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MODERN TRENDS IN THE TEACHING AND PRACTICE OF SURGERY

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THE highly technical, complex and formidable operations now commonplace in modern surgical theaters in all parts of the world represent enormous strides in the application of the healing art from the crude, bungling attempts of primitive man to arrest hemorrhage and ease the pain of trauma.

This evolution of the art and the practice of surgery through the ages is a dramatic and intriguing saga of progress which has oft-times been almost static, frequently empirical, always argumentative, but withal possessed of idealism, ambition, and humanitarianism.

Present-day surgery, representing the epitome of art and daring to venture boldly and expeditiously into all regions of the human body, has reached a point in the treatment of pathologic processes which led the late Lord Moynihan to remark: "The craft of surgery has in truth nearly reached its limit in respect both of range and safety."

The present-day type of surgery characterized by specialization, perhaps is a phase like other periods which past generations have gone through and yet as one looks back at the surgery of 75 years ago or later, one recognizes the impressions and influences which have been at work to culminate in the present methods of both teaching and practice. The loose, unorganized and sometimes sketchy type of teaching of the early part of the past century—namely by precept alone—was replaced by an institutionalized variety which in recent years has accentuated more and more the fundamental sciences and at the same time has developed many departments of specialized study.

Presidential address read before the Postgraduate Surgical Assembly, the ninth annual meeting of The Southeastern Surgical Congress, Louisville, March 8, 1938.

This change in undergraduate medical study, gradual though it was, has since 1900 undergone most rigorous and definite evolution. Reduction of medical schools by one half, elimination of sub-standard schools, and changes which have modernized the curriculum, have been indulged in, yet the fundamental principle of medical education, namely, the provision to the community of competent men in sufficient numbers to care for the sick and to forward the control and prevention of disease, has steadfastly been adhered to.

Whilst evolutionary change continues, it seems obvious that without possessing clairvoyance, the bold prophet who undertakes to predict the future of medical practice, exposes his flanks to enfilading fire, and probably, could he project his vision backward a century from now, would be humiliated by many of his prophecies which were fallacies. Nevertheless, one may by reading the trends of the times in medical education and practice, offer with not a little hesitation it is true, a prediction of the types of practice which may possibly be in vogue during the next generation.

The two most noticeable trends in medical practice to develop in the last quarter century are, first, specialization; and second, the injection of Governmental influence, both State and Federal, into control. The enormous trend toward specialization and also practice by cooperative consultation methods seem to portend that in another generation medicine may largely be practiced in urban centers at least, around (a) medical schools and teaching hospitals; (b) non-teaching hospitals; (c) loosely associated consultation groups with a central laboratory; (d) privately owned clinic groups; (e) independent consultation; and (f) general practice.

With changing economic conditions, with improving transportation facilities, with a demand for a different type of medical service, the old-fashioned practitioner, the keystone of medical practice of the past generation, is vanishing. What his general status in the mosaic of future medicine will be, I dare not venture to predict, but only express the hope that a return, at least in part, to his former status in proportion to his opportunity to serve, may reward him.

The essential changes which are now taking place and which the practice of medicine has been undergoing for a quarter of a century, demand a different policy in the matter of graduate training which supplements the undergraduate course. Actually, graduate training concerns the entire medical profession and falls readily into three groups: (1) for the specialist; (2) the research worker; and (3) that large group of medical men desiring either to change from the type of general practice they are doing, to a specialty, or who, main-

taining their present type of practice, desire to remedy their deficiencies and to keep abreast of the scientific times.

The latter group is a large, important one for many of these practitioners of a necessity find themselves engaged in the fields of both internal medicine and surgery. This is the group which will continue to be advantaged by refresher courses of short duration in graduate institutions, by attendance upon postgraduate assemblies, and by extension courses under control of state medical societies. Their whole plan of practice cannot be changed abruptly nor completely, but provision must be made for their professional stimulation and advancement by some scheme which will be incorporated in any broad plan of postgraduate instruction.

The research worker, on the other hand, represents but a small group of the medical profession as a whole. The problem of his training almost invariably is put back into undergraduate medical institutions and foundations equipped with endowments for this purpose. Graduate study should include time spent on a concrete problem in research, for few practices so develop scientific acumen, accuracy of observation and logical reasoning. Lack of time, the absence of research spirit, or both, plus the urgency of changing economic relationships, necessarily will contract the number of available research men, but they are a portion of the medical crew who should be fostered, encouraged, and stimulated to further study.

The broad field of specialization in surgical specialties presents the problem of providing opportunities for specialization as well as the recognition by the profession of qualified specialists in the different fields.

A little over a half century ago Samuel D. Gross said, "It is safe to say that there is not a medical man on this continent who devotes himself exclusively to the practice of surgery, but all medical men are general practitioners and cover the entire field of medicine, surgery, and obstetrics." No longer is such a statement true for not only is the general surgeon as he was understood in the past generation, now disappearing, but general surgery has been subdivided into multiple specialties which have rapidly divided the human body into integral parts parceled out to workers in these individual fields.

Today among physicians of the United States one out of six are full time specialists and an almost equal number give attention to or may be listed as part-time specialists. With a group representing approximately 25 to 35 per cent of the whole medical profession practicing and advocating specialization, serious consideration must be given to the development of any policy of medical education and

practice of the future which undertakes to furnish opportunities for these men to qualify themselves and at the same time attempts to regulate by certification who is and who is not a properly trained specialist. It is futile to deny that specialization is rapidly extending throughout the profession; statistical data sufficiently establish this fact. Perhaps it is the result of evolution in the development of special, highly technical procedures but since it is a definite and going concern, there is an obligation on the profession to see that the laity is protected against self-appointed and inadequately trained specialists and at the same time provided with men of competent accomplishment. Unquestionably, specialization has developed both because of a necessity and a desire on the part of both the profession and the laity, for the latter, particularly in cities, demand specialists and probably seek their advice more often directly than by reference of their own physician.

With these fundamental facts in mind about specialists and admitting a trend which seems to be increasing, the inescapable questions are, first, do we have too many specialists, and second, have we adequate means for training and qualifying specialists? The first question is easily answered, I think, if we recognize as standards of specialization, the standards of specialists themselves. We do not have an adequate number of properly trained and qualified specialists. Many practitioners in all the specialties have had too little basic and special training, and also they have not been examined and certified by an authoritative body.

Are the opportunities for training properly qualified specialists adequate? This question is answered, I think, by Manson's survey given as a part of a symposium on training in surgery before the meeting of the American College of Surgeons in Chicago, Oct. 27, 1937. He divided the hospitals to be inspected into three groups: (1) hospitals owned and operated by medical schools and generally designated, university hospitals; (2) hospitals loosely affiliated with medical schools and used for undergraduate teaching, but in which the influence of the school does not otherwise extend; and (3) hospitals having no connection with medical schools, but which might have potential facilities for graduate training in surgery. Examining throughout the year of 1937 approximately 827 hospitals, he found that 140 seemed to have facilities for graduate training in surgery and made them the subject of a special survey. By a minimum standard for rating hospitals for graduate training, 50 per cent of these, or 70, were put on an approved list, while one-third of the remainder were eligible save only for staff organization. Approximately 26 per cent of the hospitals in the survey were university hospitals, and about two thirds of the 297 residents trained

annually in the hospitals were trained in this university group. His survey seems to answer conclusively that there must be an extension of training facilities to the non-academic hospitals. Moreover, there is an optimistic note that a sufficient number of these hospitals are available to undertake graduate teaching duties if they undergo certain types of staff or service reorganization.

Recognizing then, that at present, "the weakest link in the chain of medical education is in postgraduate surgery", and that until adequate surveys have been made of all the existing facilities, it will be impossible to plan a complete program for the future, one must urgently emphasize that the hospital itself is the keystone of graduate surgical teaching. Operative experience must be provided for surgeons. No postgraduate course however long, however satisfactorily administered from the standpoint of surgical pathology and diagnosis, is complete unless the candidate actually carries out the operative act both under supervision and on his own responsibility in a sufficiently large number of cases to warrant receiving his preceptors' stamp of approval as an accomplished surgeon.

It is only fair to face the fact that these men are going to perform surgical operations, that they are licensed to do surgery, and that in consequence it is the responsibility of the profession to make them safe by providing them adequate training. The great hospitals of the teaching centers and clinics are not sufficient in number for this purpose and consequently facilities must be sought in non-academic hospitals conducted by proficient staffs under controlled conditions. At present, according to a recent report of the Council on Medical Education and Hospitals, less than one sixth of all the hospitals in the United States are approved for internships and residencies. The remaining hospitals are registered but not approved and although 1,638 of these are approved as meeting the minimum requirements of the American College of Surgeons following an inspection, the rest, or more than one half of the total hospitals, have neither been approved nor inspected by the Council of the American Medical Association or the College of Surgeons. Obviously, in this group of hospitals there will be many in which part or all of the necessary training for certification as a surgeon can be obtained for a limited number of men. Undoubtedly, the vast majority of surgeons must still be trained in the teaching centers and the hospitals located in large urban centers.

Recently fostered by the American Surgical Association and participated in by sectional surgical societies, the Surgical Section of the American Medical Association, and the American College of Surgeons, the American Board of Surgery was organized. The avowed

purpose of this Board is to increase the opportunities for surgical teaching and to elevate the standards of surgery.

The American Board of Surgery established the minimum requirements of four years of hospital or institutional training, supplemented by a further two-year period of study or practice as an experimental plan worthy of trial. It is less liberal than the requirements for a Fellowship in the American College of Surgeons and not so rigorous in many respects as the requirements of the Royal College of Surgeons of England. Interest in this Board is evidenced by the fact that 267 young surgeons applied for the privilege of taking the first examination held Oct. 20, 1937, and of this number, 109 were considered to have fulfilled satisfactorily the requirements set down by the Board as constituting eligibility for the examination.

A further significant fact is that more than 700 members of the Founders' Group, representing the senior surgeons of the United States have approved the principles and proposals of the Board and have accepted certification. All of these efforts at increasing surgical proficiency demand cooperation between the major professional groups and particularly those groups which control hospitalization. Knowledge of the exact facilities for conducting graduate training has been meager in the past, but as recently as 1934 the American College of Surgeons appointed a Committee for the study of graduate training in surgery.

The Council on Medical Education and Hospitals of the American Medical Association has even more recently launched a campaign to make a comprehensive study of all phases of graduate medical education. A Commission of Graduate Medical Education, authorized by the Advisory Board of the Medical Specialties, has been created to mobilize current opinion as to how the problems in this field can best be solved, and to formulate the fundamental principles involved in medical graduate training. This Commission headed by the Dean of Columbia University, College of Physicians and Surgeons, is comprised of representatives of the medical profession, hospitals, universities, medical schools, and licensing bodies. It is a reasonable hope that out of its efforts will develop a philosophy of professional study which will implement changes consonant with fluctuant conditions and integrated with modern plans of medical education.

These concerted programs by different national bodies evidence the intense interest the medical profession has in not only assembling satisfactory data concerning the facilities for increasing the efficiency of graduate training and affording more opportunities to more men for training, but the desire to coordinate efforts and cooperate with each other. By the same token these authoritative bodies comprised

of determined, forward-looking members of the profession, by collecting this information relative to our present facilities, promise a definite plan for the future which will be practical and workable for the education of a specialist in any particular field.

The second major trend which is unquestionably influencing the present-day practice of medicine and probably will project its shadow largely into the future unless there is marked deviation from its apparently charted course, is the attempt of Government to subsidize and control health services. Efforts of persistent, persuasive, purposeful, probably public-minded, but certainly politically-controlled, pressure groups to extend public health agencies and to dominate, under Governmental auspices, medical service, if successful, will bring us nearer and nearer to some modified state of socialized practice. That this is a menace intolerably abhorrent to the majority of practicing physicians is beyond controversy. Bureaucratic control, whether by State or Federal agencies, inevitably, if one may judge by the experiences and reports of Continental attempts at socialization of medicine, results in a lowering of the standards of professional care and most certainly obtunds the ambition and interest of the practicing physician.

It is unbelievable that socialization of medicine as the picture is usually projected, is an immediate possibility in the United States, nor can one willingly accept the thesis that it is a necessary part of an evolutionary socio-economic scheme to which we are apparently committed. Science knows no territorial boundaries nor does it consider race, creed, or social conditions. The practice of medicine in this country has rested securely in the hands of organized medicine for centuries and while there may be justification at times to chafe at what appears to be ultra-conservatism, it is well to remember that in times of change it is improbable, indeed it is foolish to assume, that any socio-political agencies should have at heart the improvement of the nation's health more than scientific bodies. It is equally as unlikely that these groups are better able to estimate and forward any movements to improve the general status of the public's health than those whose every-day task it is.

It may well be pointed out that, despite charges of proponents of radical change in medical practice, there is no obstruction on the part of the organized medical profession, to progress, nor is there a tendency to be reactionary in method. Under no compulsion from any source, the medical profession has continued through many vicissitudes, extending back into the remote ages to follow a charted course of advancement which has resulted always in elevation of standards both of education and practice in both curative and preventive medicine. Continually is the medical profession subjecting

its methods of practice to careful, painstaking, and unbiased scrutiny, and demanding of its adherents a higher grade of efficiency. The reduction of infant mortality, the advances in combating communicable diseases, the increase of life expectancy throughout the past century, and the wholehearted support of the present movement within its own ranks to certain qualified specialists, are samples of the noteworthy accomplishments which refute many of the accusations of its critics.

That the present turbulent social unrest throughout the world which fortunately is less urgent in the governmental set-up of democracies of the Western Hemisphere than in the Old World, necessitates certain changes in medical practice, is admitted by all. That governmental systems giving funds raised by taxation could be advantageously integrated with the present system of caring for the indigent and near indigent and without subsidizing the service is, I believe, hardly debatable for ample evidence of satisfactory cooperation between agencies controlling funds for public institutions such as city hospitals, and for the support of medical education and research in departments of certain large universities as well as the extension of the U. S. Public Health services, is not lacking.

Many arguments for cooperation and coordination of Governmental agencies and the present system of practice of medicine may be advanced. However, an enormous amount of study and correlation of data must inevitably be done before a definite decision on the necessity of change of any magnitude in today's present system of practice is arrived at.

No medical man would object to changes in medical practice which were advantageous to the nation's health and which beyond cavil were not politically fostered, dominated, and directed. The medical profession has no disinclination to aid and cooperate with authorities whose aim is improvement of the health of the underprivileged, but the extension of a health program which is all-inclusive and controlled by Federal authorities wholly or in part, seems an extraordinary procedure distinctly open to question. This proposed extension is summarized in the words of an enthusiastic proponent as follows: "The issue is, to put it sharply, whether government shall more properly concern itself with the relief of one group of the population, the underprivileged, in illness, or whether it shall concern itself with better health for all groups of the population, the privileged and the underprivileged alike." Socialization of medicine may be, by the terms of the definition given by the House of Delegates of the American Medical Association in 1922, designated as any form of medical service, diagnosis, or treatment which is con-

trolled by Government, Federal or local, with certain exceptions which include the armed services, public health services as well as communicable and mental diseases, and locally administered services by county medical associations with the approval of their state associations.

The main objections to state-managed medicine fall into three categories: first, the huge increase in the cost of medical care; second, the decline of medical services; and third, the abuses both political and professional which this type of service encourages. The economic considerations under even mild scrutiny indicate a great increase in the cost of medical care due to enormous administrative expenses. If one may judge by any standards of Governmental control hitherto imposed, this is an inescapable conclusion.

To the second proposal that medical services depreciate under bureaucratic control, one need only point to the incontrovertible facts that mortality and morbidity are not reduced, graduate education and study decline, research languishes, political issues become predominant, and human values secondary.

A united front by organized medicine must be presented to these proponents of political domination and agitators for cataclysmic changes in the present-day type of practice. The medical profession itself has a concrete answer to socialization in the type of service it renders to the community. Its obligation is to continue to practice good medicine, and to advance the cause of preventive medicine and research in the full realization that the care of the sick is the paramount duty of the doctor.

Any system which places medical service in a position to be influenced by political expediency and opportunism inevitably forces scientific bodies under the control of non-medical agencies and defeats the professed idealism of the ambitious advocates of health control outside of professional medical organizations. With a reduced type of service, with an increased cost, with a consideration of the experience of European countries which have adopted some form of socialized medicine, all repugnant to the individualism of a true democracy, shall we not consider well before any visionary, untried schemes in this country make us deviate from the well-tried methods of practice handed down to us from the pioneers of our guild?

The medical profession thinks in terms of orderly, evolutionary processes of progress and believes that these accomplishments should be carried out in regular and thoughtful sequence.

The health of the nation is safe in the hands of the medical profession.

INTRAOCULAR TUMORS

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OUR problem in ophthalmology in regard to intraocular tumors is to determine whether or not a tumor exists in an eye. As a biopsy is never possible, and as there are so many conditions that simulate an intraocular newgrowth, this problem is often very difficult. If we conclude that a primary neoplasm is present in the eye of an adult, then it is with extremely rare exceptions, a malignant melanoma of the choroid. If we conclude that a primary neoplasm is present in the eye of a child then it is a glioma of the retina. It is therefore usually more difficult for us to state whether a tumor is present than what kind.

Practically speaking, the tumors that are encountered in the eye are limited in order of frequency to benign and malignant melanoma of the choroid, glioma of the retina and metastatic carcinoma of the choroid. These would no doubt comprise 95 per cent of the cases. Among the rarer tumors there are malignant melanoma and metastatic carcinoma of the ciliary body and iris, hemangioma of the choroid, etc. Primary carcinoma in the eye is practically unheard of. Only the more frequently encountered ones will be considered here.

Benign melanomas of the choroid are common (Fig. 1). However, they are frequently overlooked in the examination of the fundus because the pigment epithelium obscures them more or less from view. They appear clinically as flat to slightly elevated, poorly demarcated, slaty-gray to brown areas which vary widely in size and shape. It is probably from these that malignant melanomas arise and make their presence known to the patient by a disturbance in the visual field (Fig. 2).

They often present difficulties in diagnosis. The retina is frequently detached over the lesion instead of being pushed out. Thus the presence of the globular mass beneath it, along with the usual pigment content, cannot be easily appreciated. Or, the tumor may grow exceptionally flat and contain little or no pigment. Sometimes secondary glaucoma or a cataract or both may be present, producing cloudy media, which interfere with accurate observation.

Occasionally a choroidal melanoma overgrows its blood supply and becomes necrotic. This disintegrated tumor tissue is quite toxic

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Read before the Postgraduate Surgical Assembly, the ninth annual meeting of The Southeastern Surgical Congress, Louisville, March 7, 8 and 9, 1938.

and produces an inflammatory reaction in the eye which simulates clinically an endogenous endophthalmitis. This reaction may be so severe that it spreads out of the eye to the orbit giving an orbital cellulitis and exophthalmos (Fig. 3). The cloudiness of the cornea, caused by the inflammation, frequently secondary glaucoma, cataract, or both, prevent a view into the interior of the eye and thus the diagnosis can be quite difficult. Therefore, an unexplained unilateral endophthalmitis or panophthalmitis in an elderly person should lead one to suspect the possibility of a necrotic melanoma.

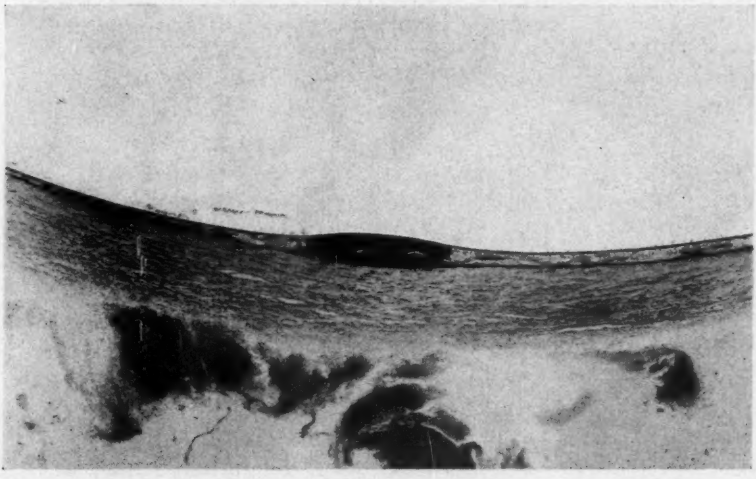

Fig. 1. Benign melanoma of the choroid.

In such instances, in order to make the diagnosis, one must rely on means other than merely the clinical appearance of the lesion. In this regard, transillumination is very important. In my opinion, the transilluminator devised by Professor Lange gives decidedly the best results and is a necessary requisite to any ophthalmologist's equipment.

The presence of a cataract does not interfere with the test. In carrying out the test, a local anesthetic should be instilled in the conjunctival sac and the point of the instrument placed at various sites against the sclera far back in the culdesac. The light is thus transmitted freely through the pupil except when the point of the instrument is over the site which interferes with the light transmission. If the lesion is posterior to the equator of the globe, erroneous results may be obtained if the point of the instrument is at the equator or anterior to it. The point of the instrument should be at

the center of the lesion or even more posterior. If the lesion is near the posterior pole it may even be advisable to place the instrument over the site of the lesion by making an incision in the conjunctiva. In observing through the dilated pupil for any interference in the transmission of light, it is advisable to use a binocular loop, although this is not absolutely necessary. In order to strike the incident rays as they emerge through the pupil, it is frequently necessary for the observer to shift his head.

I have noted repeatedly the presence of localized accumulations of pigment cells along the anterior surface of the iris in eyes which

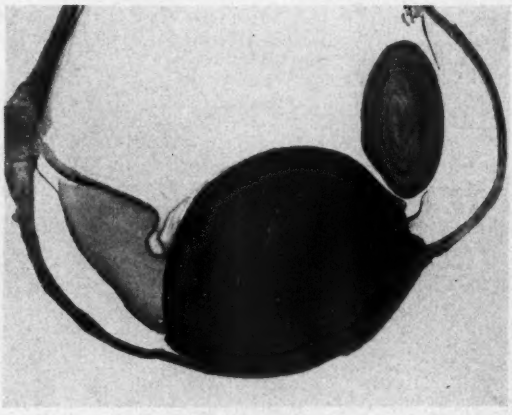

Fig. 2. Malignant melanoma arising in the choroid and extending forward into the ciliary body. Between the optic nerve and the tumor the retina is detached.

contain a malignant melanoma of the choroid. When these small melanomas, or "freckles," are noted on the iris of an eye in which a malignant melanoma is suspected, then it is substantiating evidence when such melanomas are not present in the fellow eye. This point was quite helpful in the correct diagnosis of a case recently where the diagnosis of a choroidal melanoma was doubtful.

A melanin test of the urine is usually done, but I have never been convinced of its value.

A differential diagnosis must be made between malignant melanoma of the choroid and several other conditions:

1. In every case of detachment of the retina, the presence of a melanoma of the underlying choroid should be ruled out. When the transillumination is good, and there is a history of trauma, myopia is present, a hole in the retina is seen, etc., a diagnosis of simple serous retinal detachment can be made.

2. A hemorrhage of the choroid, subretinal space or vitreous can simulate a choroidal melanoma. A differential diagnosis can be difficult as hemorrhage interferes with transillumination, and when it has been present for some time it may undergo hemosiderin changes which add the element of pigment to the lesion. Such hemorrhages are frequently present in patients with diabetes, high blood pressure and arteriosclerosis.

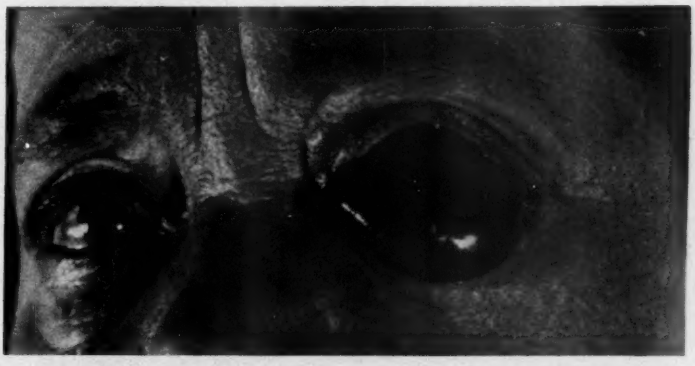

Fig. 3. A severe inflammation of the eye and adjacent orbital tissue (exophthalmos of 4 mm.) caused by the toxic effect of a necrotic malignant melanoma of the choroid. The bullous mass protruding between the lid margins is edematous conjunctiva. The interior of the eye could not be seen and there was no evidence of the existence of the newgrowth from the external examination.

3. Detachment of the choroid may result from operations for cataract and glaucoma, or perforating injuries. It reattaches usually in the course of weeks. As a detached choroid protrudes as a globular mass which is dark in color, it resembles a choroidal melanoma. I know of one instance where a patient was seen with acute glaucoma for which a Lagrange operation was performed. Immediately following the operation the surgeon saw a lesion in the eye which he thought was a malignant melanoma of the choroid and he enucleated the eye. This proved to be a detachment of the choroid.

4. Metastatic carcinoma of the choroid will be discussed elsewhere.

In performing an enucleation for melanoma of the choroid, it is not particularly important to secure an exceptionally long segment of the optic nerve as this tumor has no tendency to spread into the nerve. When the growth extends out of the globe, it is by way of

the emissaria through which the ciliary arteries and nerves traverse the sclera. Thus, nodules of the new growth, which are often fairly well encapsulated, may be along the external scleral surface in the region of these emissaria. If, at the time of enucleation, the orbital tissue is dissected from the scleral surface without cognizance of the possible existence of such extraocular extensions of the growth, some of the tumor tissue may be left in the orbit. After the globe is delivered from the orbit, and we see from inspection that there has been no gross extraocular extension, which has been interfered with in the dissection, then we do not hesitate to employ a gold-ball implant. It is an extreme rarity to have a melanoma recur in the orbit. In fact, it has been said that the prognosis is as good in those cases in which there has been an extraocular extension as it is in those in which the tumor has remained within the globe.

We have just completed a follow-up of 64 cases of malignant melanoma of the choroid enucleated during the period between July, 1929, and October, 1936. Ten of these could not be traced. This leaves a total of 54 which were accounted for as follows: 39 patients reported they were well, 3 showed evidence of metastasis, 8 had died of metastasis, and four of other causes. This gives a mortality of 20.4 per cent.*

In 1930 enucleation was done on 3 patients, 2 of whom were well and 1 died of other causes;

In 1931 enucleation was done on 1 patient who died of generalized metastasis after 1 year;

In 1932 enucleation was done on 9 patients, 8 of whom were well and 1 developed a metastasis;

In 1933 enucleation was done on 13 patients, 9 of whom were well; 3 died of metastasis within 2 years, and 1 died of other causes;

In 1934 enucleation was done on 9 patients, 6 of whom were well; 1 died of metastasis after 6 months, 1 has very recently developed pain in the region of the stomach suggestive of metastasis, and 1 died of other causes;

In 1935 enucleation was done on 10 patients, 7 of whom were well; 2 died of metastasis in 2 years and 1 of other causes;

In 1936 enucleation was done on 8 patients, 6 of whom were well; 1 developed a recurrence in the orbit, and 1 died of other causes.

This tabulation of our cases brings out the fact that if the new growth proves fatal, it is usually within two years' time.

*As five years is considered the minimum that should elapse before reporting results in cases of cancer, this figure should not be accepted as final in this series.

Callender and Wilder have developed a special silver stain which shows the argyrophil fibers of these tumors. From a series of 120 cases, followed not less than one year, they feel that a more accurate prognosis is indicated according to the prevalence of these fibers.

They divided their cases into the following groups:

1. No argyrophil fibers among the tumor cells.
   Mortality 57 per cent.
2. Partially fibered—
   a. Less than 50 per cent argyrophil fibers.
      Mortality 42 per cent.
   b. About 50 per cent argyrophil fibers.
      Mortality 37 per cent.
   c. More than 50 per cent argyrophil fibers.
      Mortality 22 per cent.
3. Argyrophil fibers throughout all areas.
   No mortality.

Forty-six cases were followed five years or longer, or death occurred within five years, and of this series, the following statistics were compiled.

1. No argyrophil fibers.
   Mortality 100 per cent.
2. Partially fibered—
   a. Less than 50 per cent fibered.
      Mortality 87 per cent.
   b. About 50 per cent fibered.
      Mortality 76 per cent.
   c. More than 50 per cent fibered.
      Mortality 22 per cent.
3. Fibers throughout all areas.
   No mortality.

Retinoblastomas* occur in infants and young children. They may be congenital tumors but unrecognized until a sufficient time after birth has elapsed for them to grow large enough to produce a visible white reflex in the pupillary area (Fig. 4). Both eyes should be examined very carefully as in 25 per cent of the cases the lesion is bilateral. This does not mean that the tumor has spread from the one eye to the other via the optic nerve and chiasm but that the tumor is of multiple origin. It often shows also multiple origins in the same retina. Secondary glaucoma with its accompanying pain and redness may be the first sign of the existence of

*The term "glioma of the retina" is a misnomer because the tumor arises from the nuclear layer of the retina and not from the glia or neuroglia. It has been suggested that the term "retinoblastoma" supplant the old and established term of glioma.

the tumor. They may simulate closely other conditions and the presence of glaucoma and cataract may complicate the picture.

Aids therefore in diagnosing these tumors are in order. Transillumination is not interfered with as much as it is in malignant melanoma of the choroid but the use of it in making the correct diagnosis is important. It is necessary to give the patient a general anesthesia for a satisfactory examination.

An important point in diagnosing these tumors is the presence of pearly-white, fairly sharply demarcated foci of varying sizes tending to aggregate themselves over the surface of the lesion. These represent calcium deposits which are a common characteristic. Pfeiffer has shown that these areas of calcium are frequently demonstrable by x-ray. When they are seen clinically or in the x-ray, they are pathognomonic of retinoblastoma.

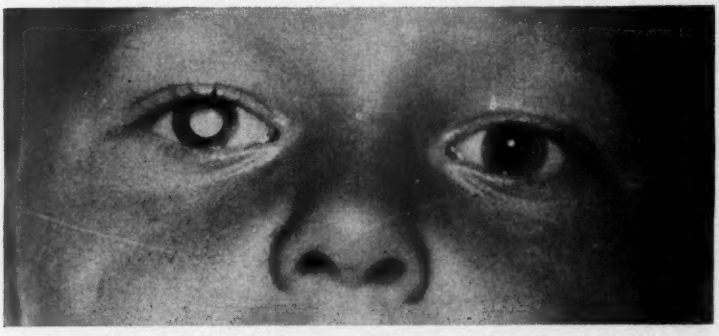

Fig. 4. The white pupillary reflex in the right eye caused by a retinoblastoma in a boy aged 4 years. In one year this patient showed a metastasis in the bones of the skull and later throughout the entire body.

Fragments of the tumor sometimes become free and migrate to various sites within the eyeball. They may be seen clinically sometimes as globular masses floating free in the vitreous. Sometimes these fragments rest on a vascular structure like the surface of the choroid, ciliary body or iris, and there grow as implantation growths. When these implant themselves and grow along the anterior surface of the iris they can be seen clinically and are naturally an important point in the diagnosis.

The tumor may become necrotic through outgrowing its blood supply and thereby tend toward or actually accomplish a spontaneous cure. The necrosis thus produced may cause sufficient inflammation to lead to phthisis bulbi. There are other conditions which produce a similar white reflex in the pupillary area and the differ-

ential diagnosis can sometimes be difficult. To this group of pseudo-retinoblastomas belong metastatic retinitis, organized intraocular hemorrhage occurring at birth, congenital remains of the embryonic vascular capsule of the lens and Coats' disease.

The metastatic retinitis more often occurs during one of the exanthematous diseases, but due to its mild character it is only detected a long time afterwards when organization leads to a detachment of the retina which is drawn up by contracture of the scar tissue into a mass posterior to the lens, thus giving the white reflex.

A massive intraocular hemorrhage may occur at birth due to the congestion of the jugular area, particularly occasioned by a long labor, or by trauma from instrumental delivery. This is comparable to the intracranial hemorrhage of the newborn, both belonging to the same venous system. The massive hemorrhage in the retina organizes into a white mass which may resemble a retinoblastoma.

The vascular capsule which envelops the lens in embryonic life should disappear a short time before birth. When this fails to occur it is on the posterior surface of the lens that the tissue remains. It therefore appears as a white mass in the vitreous and thereby resembles a retinoblastoma.

In performing the enucleation, it is important to secure a long optic nerve as retinoblastomas spread into the optic nerve beyond the lamina cribrosa in 52 per cent of the cases. After the enucleation, the excised optic nerve should be prepared immediately as biopsy tissue to determine whether or not the tumor has extended into the nerve beyond the site of the excision. If so, radiation should be started immediately.

If the tumor is bilateral, it is usually much more advanced in one eye. The vitreous cavity is partially filled with tumor and immediate enucleation is indicated. The lesion in the fellow eye is usually much less advanced and there is still a good, functioning eye. In such instances roentgen radiation should be given, using multiple small portals 7.5 cm. in diameter, adhering to accurate direction of the beam of roentgen radiation, employing multiple treatments, sometimes even up to as many as 75, and over a long period of time, even as long as eighteen months in some instances.

The Division of Ophthalmic Pathology of the American Registry of the Army Medical Museum has reported on 95 cases of retinoblastoma which were proved microscopically following the enucleation of one eye. Twenty-six of these were bilateral and 69 unilateral. Thirty-nine patients died, 10 were living after one year, 6 after one to two years, 4 after two to three years, 2 after three to four years

and 13 over five years. The status of 21 was unknown. This gives a mortality of 52 per cent.

The prognosis for the bilateral cases, in which one eye was enucleated and the other radiated, according to the technic previously described, cannot be given satisfactorily because a sufficient number of cases have not been radiated. From a consecutive series of 8 cases, reported by Martin and Reese, there appears to be, after two to three years, an arrestment of the disease in approximately 50 per cent of the eight cases.

In the follow-up of these cases, one should look for recurrences locally in the orbit and in the bones of the body. A firm nodule along the surface of the flat bones of the skull is frequently the first sign of metastasis.

The commonest primary sites for carcinoma which metastasizes to the eye are the breast, thyroid and stomach. The carcinomatous emboli implant themselves most frequently in the choroid and less frequently in the ciliary body and iris. They never occur in the retina. It is interesting to note that infectious emboli implant themselves commonly in the retina. The reason for this difference in location for the neoplastic and the infectious emboli seems to be due to the fact that the neoplastic emboli are larger and therefore roll along the vessel walls in the periphery of the blood stream. They therefore are carried off into the posterior ciliary arteries which are the tributaries of the ophthalmic artery. The infectious emboli are smaller and therefore course in the center of the blood stream. They thus continue on to the terminal central retinal artery and implant themselves in the end artery system of the retina.

A metastatic carcinoma to the choroid manifests itself in a disturbance of vision. Often this is rather marked due to an extensive detachment of the overlying retina. The metastatic focus tends to grow flat and therefore any detachment of the retina over this frequently gives the appearance of a simple serous detachment. The diagnosis is readily suspected when the patient is known to have a primary focus elsewhere. It is not uncommon though for the metastatic carcinoma in the eye to manifest itself by visual disturbance before the primary focus is known to exist. I have seen a patient with metastatic carcinoma to the choroid of both eyes and a most thorough search for the primary site failed for some time until finally a nodule became palpable in the thyroid. This enlarged rapidly and a biopsy showed primary carcinoma. In two other instances the primary sites were not found for some time after the metastatic focus manifested itself in the eye. The one proved later to be pri-

mary in the lung and the other proved at autopsy to be primary in the stomach. Therefore, in any case of detachment of the retina, the possibility of a metastatic carcinoma being the underlying cause must be kept in mind.

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SULFANILAMIDE

I. General Discussion of the Drug

II. Sulfanilamide with the Sealing Treatment of Beginning Gonorrhea

III. Sulfanilamide in Combination with Artificial Fever

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I. GENERAL DISCUSSION OF THE DRUG

BECAUSE the list of dependable therapeutic drugs is regrettably short most of us are therapeutic skeptics. It is a surprise, therefore, to find a new drug as potent as sulfanilamide. Its chemical name is para-amino-benzene-sulfonamide. A trade name is prontylin.

Sulfanilamide may well be called a chemical of surprises. It is surprising that a drug useful in so many infections should have aroused so little interest when it was first made that the method of its manufacture was not even patented.

It is surprising that so little is known of its early use in chemistry and therapeutics.

It is surprising that it is potent in both acid and alkaline media and for certain bacilli as well as cocci, but not for spirochetes.

It is surprising that sulfanilamide can assist in the destruction of so many bacteria and yet permits, at times, organisms to remain alive for a considerable time and to produce recurrences.

It is surprising that a chemical so slightly soluble in water and one so mildly germicidal in experimental test tube work, should have proved so efficacious in the treatment of infections in the animal as well as in the human body, and that it should reach its peak of blood stream saturation within about five hours after its administration by mouth.

It is surprising that its administration by mouth affords better results than when it is given intramuscularly.

It is surprising that it has such a variety of disturbing by-effects

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and equally surprising that the majority of them should disappear promptly after it is discontinued.

It is surprising that its mode of action is so elusive that scientists are still uncertain as to the manner in which its curative action takes place.

It is surprising that, for instance, an agent as potent as sulfanilamide in controlling the inflammatory process of otitis media, should not be efficacious in rendering the secretion from the ear sterile.

It is surprising that patients with gonorrhea, responding well to treatment with sulfanilamide, should harbor gonococci in urethral shreds long after symptoms of the existing infection have ceased.

It is surprising that nearly all cases of early gonococcic urethritis can be promptly cured by combining proper doses of sulfanilamide with the sealing of a 5 per cent solution of mild silver-protein (argyrol) in the anterior urethra on four successive days, whereas a comparatively high percentage of failures occur when either procedure is used alone.

It is surprising that a pocketed focus of infection, such as prostatitis, should respond as well as it does to treatment with sulfanilamide.

It is surprising that many infections which have been resistant to treatment with sulfanilamide alone will disappear in about 90 per cent of the patients when this remedy is used in combination with artificial fever.

It is not surprising that sulfanilamide occasionally causes agranulocytosis. This toxic effect on the blood forming mechanism was predicted early on account of its chemical structure.

Perhaps there is to be another surprise in the recent discovery by Dochez and Slantez, of a distant relative of sulfanilamide, known as sodium sulfanil sulfanilate. This drug appears to be a specific for the animal virus which causes distemper in dogs and cats. Apparently, it may find a place later in the treatment of more or less similar conditions which are caused by ultramicroscopic viruses in man.

Time will not permit a discussion of the hazy early history of sulfanilamide and its chemical synthetic cousins.

Practically all of the chemicals closely allied to sulfanilamide break down in the body into this drug and are largely eliminated as such in the urine.

So far no new preparations have been found which are better

than sulfanilamide. In fact, they all seem dependent upon reduction to sulfanilamide for their therapeutic effect.

That sulfanilamide is secreted by the prostate gland of the dog in sufficient concentration to kill the colon bacillus in 24 hours has been demonstrated very recently by Farrell, Lyman and Youman. For their experimental work dogs were selected because of their relatively large prostate glands. Thus was shown experimentally the reason why posterior urethritis and prostatitis are prevented or have benefited by sulfanilamide therapy.

Theories as to the Mode of Action of Sulfanilamide

How does sulfanilamide assist in the eradication of bacteria from the blood stream and elsewhere in the body? In spite of much experimental study the answer to this question still remains unsettled. Some workers believe the action of sulfanilamide is in stimulating phagocytosis. Others belileve its action is in the serum through opsonic activation; and still others think it acts in a manner somewhat similar to that of an antitoxic agent.

Even a summary of much interesting experimental work being carried on by numerous investigators is not permitted.

It is our personal opinion, though, that the bacteriostatic action of sulfanilamide, when it reaches a suitable concentration in the blood stream, acts by lessening the toxin produced by the bacteria, rather than by neutralization of toxins already produced. This seems plausible and is in harmony with clinical results. If the beneficial effects of sulfanilamide were truly antitoxic the results from its use would be expected to appear promptly instead of 24 to 48 hours after adequate administration of the drug.

What we personally think happens is that the bacteria, attenuated by sulfanilamide, produce less toxin than normally. Being less toxic when sickened by sulfanilamide, bacteria appear to undergo phagocytosis more readily than they do when not so handicapped. In every day language the weakened organisms seem more palatable to the phagocytes and are less harmful to them when ingested. This opinion is supported by the work of Osgood and his associates who have recently carried out extensive experimental studies of the action of sulfanilamide on bone marrow cultures of the beta hemolytic streptococcus. They conclude that sulfanilamide has no direct effect on phagocytosis and that its major action seems to be antitoxic. This appears to bear out our opinion that weakened bacteria are themselves less toxic and therefore are more readily incorporated by the leukocytes which in turn remain more active in their phagocytic role.

This view also has a practical importance, namely that sulfanilamide must be continued for a sufficient period of time to allow for adequate phagocytosis or whatever its curative property is. Attenuated by sulfanilamide, many susceptible bacteria tend to become harmless parasites which are controlled and finally killed by the leukocytes or by the bactericidal property of human serum. It is logical and borne out by practical experience, therefore, to continue treatment with other agencies and with sulfanilamide, in gradually decreasing dosage, until sufficient time has been permitted for complete eradication of the offending organism. At a later date we hope to present data which will show that the amount of toxin metabolized and given off by attenuated bacteria is less than that of bacteria not influenced by the bacteriostatic action of sulfanilamide.

Clinical Uses and Methods of Administration of Sulfanilamide

Many infections have responded to sulfanilamide: among these are puerperal septicemia, erysipelas, pharyngitis, tonsilitis, sinusitis, septicemia, streptococcic and gonococcic arthritis, otitis media, scarlet fever, peritonitis, gas gangrene, acute endocarditis, malaria, lymphogranuloma inguinale, undulant fever, gonococcal infection, and especially infections due to the streptococcus hemolyticus.

For urinary infections, gonorrhea as well as others, the oral administration of sulfanilamide in 5 grain tablets is the best. The dosage should vary according to the nature and severity of the infection and should be gauged in proportion to the age, weight, physical condition and tolerance of the patient. Naturally there must be a wide range as to dosage. The average patient, especially those confined to bed or hospitalized, tolerate sulfanilamide fairly well, much better in fact than they tolerate ketogenic diet or mandelic acid. About 10 to 20 per cent, however, are unable to take it satisfactorily.

The tendency of sulfanilamide to induce acidosis requires the simultaneous administration of an alkalinizing agent such as bicarbonate of soda and in an amount sufficient to render the urine neutral or alkaline in reaction.

For fairly husky adults 15 or 20 grains of sulfanilamide may be given four times a day, preferably after meals and at bed time. Within two or three days, or as soon as decided clinical improvement has resulted, the dosage should be reduced by about one fourth or one third for a period of five days and thereafter continued in smaller doses for some time. Recurrence is likely if the drug is stopped as soon as the symptoms abate and if supplementary measures are neglected.

A definite though variable concentration of sulfanilamide in the blood is required. Alyea, at Duke University, at first thought failures were due to the lack of such concentration. In this he found he was wrong since there were failures in the treatment of gonorrhea when the concentration was adequate. Then he thought poor results were due to failure of the body metabolism to conjugate the sulfanilamide properly or normally. But he soon found he was wrong in this too. At present we cannot say why in certain patients the infection fails to respond to sulfanilamide even though the drug is well tolerated in adequate doses.

Toxic Effects of Sulfanilamide

A great variety of minor reactions follow the use of sulfanilamide. These include loss of appetite, dizziness, malaise, a sensation such as usually follows alcoholic intoxication, a "jittery" feeling, faintness, difficulty in breathing, etc.

Fever and skin rashes, more or less like scarlet fever or measles, are not uncommon, but usually clear up promptly upon cessation of sulfanilamide. These skin rashes as a rule occur in the part of the body most exposed to sunlight, either before or after the administration of sulfanilamide. So far during the winter months we have not seen a patient with such skin complications, while last summer these rashes were seen not infrequently.

Cyanosis, due to methemoglobinemia or sulfhemoglobinemia, is of common occurrence but does not necessarily need to be regarded as an indication that treatment should be discontinued. The mode of origin of these inert forms of hemoglobin is not known positively but sulfate cathartics, probably through unusual amounts of hydrogen sulfide, are thought to play a part in the production of sulfhemoglobinemia. For this reason such cathartics are contraindicated during the administration of sulfanilamide. Methemoglobinemia yields more readily to oxygen therapy than does sulfhemoglobinemia which may require venesection followed by transfusion. Cyanosis sometimes is present without sulfhemoglobinemia or methemoglobinemia.

The carbon dioxide combining power of the blood is always reduced by sulfanilamide. On this account, as already stated, an alkalinizing agent such as sodium bicarbonate is given to prevent acidosis.

Fever, occasionally associated with abdominal cramps or pain, sometimes results from sulfanilamide. Cessation of the treatment for a few days may become necessary to determine if the fever is from the disease or from the remedy; if the latter, the resumption of sulfanilamide should be watched carefully.

Hemolytic anemia is a serious by-effect of sulfanilamide occasionally seen; whether this is a toxic effect or due to an idiosyncrasy is not known. When it occurs it should not be confused with the far less serious cyanosis previously mentioned. If hemolytic anemia should arise sulfanilamide should be discontinued and blood tonics and liver extract should be administered. Tranfusions should be employed if a marked reduction in the red cells has occurred. If a patient with a decided anemia is in need of sulfanilamide it is not necessarily contraindicated but during its administration the red cells and hemoglobin should be watched with great care.

The most serious result of sulfanilamide, but fortunately not a common one, is granulocytopenia. When this disease occurs it is usually fatal in spite of medical care. It is not practical to make blood counts constantly on all patients taking sulfanilamide but such studies should be made promptly in all who are not doing well or who show untoward symptoms. It is of the utmost importance that physicians using sulfanilamide should inform themselves as to the great variety of toxic effects of this surprising drug.

For patients who are vomiting and cannot take tablets of sulfanilamide, intramuscular injections in the form known as prontosil solution, may be administered. It is practically non-irritating and is rapidly absorbed. The slight stinging produced at the site of injection soon subsides. The dose for an adult of average size is 20 c.c. This should be repeated every four hours. It should be continued in this dosage, unless toxic symptoms appear, until clinical improvement becomes evident. The amount may then be decreased. This is the dosage recommended for severe streptococcic infection. Smaller doses should be given in milder infections.

Sulfanilamide may be given in physiologic saline by hypodermoclysis. Long and Bliss recommend 500 c.c. of an 0.8 to 1.0 per cent solution of sulfanilamide as the initial dose for the average adult, followed by 300 c.c. doses at 8 hour intervals for the first 24 hours; subsequent dosage should be regulated according to circumstances.

Sulfanilamide in 0.8 per cent solution is not irritating to the meninges and in the treatment of streptococcal meningitis may be given intrathecally after spinal drainage, just as antisera are given. The amount of solution administered is 5 or 10 c.c. less than the amount of spinal fluid withdrawn. The solution is allowed to flow into the spinal canal by gravity and may be repeated at 8 hour intervals.

Therapeutic Results from Sulfanilamide Therapy

It is impossible to give at the present time a satisfactory statistical summary of the results of sulfanilamide because of the wide diversity of opinion as regards dosage. Furthermore, some have given sulfanilamide alone, while others have supplemented its use with other measures.

Practically all, however, are agreed that the complications of gonorrhea are greatly reduced by the administration of sulfanilamide. In about one-third to one half of the patients the time required for eradication of the infection is decidedly reduced. In about one-fourth the duration of gonococcic infection is not influenced but the symptoms are less disturbing than usual, so much in fact, that Clark and others have emphasized the dangers involved by the false sense of security thus incurred. Undoubtedly great care is required in deciding when such patients are free from infection. About 10 to 20 per cent of patients are unable to take curative doses of sulfanilamide.

Finally, there is a good sized group of patients in whom sulfanilamide is of little or no value, even when adequate doses are tolerated.

Undoubtedly many doctors have left off the drug because of unpleasant but unimportant toxic reactions, while others have continued large doses in spite of less disturbing danger signals.

Our own experiences with sulfanilamide have been gratifying. We have, however, employed it along with other routine therapeutic measures and until adequate tests showed that the patients were free from infection.

Sulfanilamide is not readily excreted by kidneys with poor function, and in such cases smaller doses may bring the concentration in the blood stream to an adequate degree for therapeutic results in systemic infections but not in those of the urinary tract. For the same reason, though, dangerous toxic effects are likely to arise from the usual dosage in patients with poor renal output.

Our results with sulfanilamide in the treatment of ordinary bladder and kidney infections often have been excellent, especially when such infection was not caused by, or associated with, obstructive lesions at the bladder neck or in the ureters. The existence of urinary stasis or stones is much more likely to be the cause of failure than is the presence of resistant strains of bacteria.

Adequate blood stream concentration is needed for systemic and local infection. Concentration in urine is equally needed in urinary infections. Consequently, the intake of fluids should be restricted.

II. Sulfanilamide in Combination with Argyrol Sealed in the Anterior Urethra for Recently Acquired Gonococcic Infection

When we see gonorrhea patients whose discharge has been present for not more than two days, and in which the incubation period has been within the range of normal, exceptionally satisfactory results have followed the oral administration of sulfanilamide, combined with daily treatment, for four days, with 5 per cent solution of mild silver-protein sealed in the anterior urethra.

The treatment is administered as follows: After the patient has voided and the meatus and glans penis cleansed, about 20 minims of a freshly made solution of 5 per cent argyrol is injected into the anterior urethra where it is held in place with a clamp. The meatus is then dried thoroughly and coated with plain U. S. P. collodion applied with a camels hair brush. The patient remains prone until the collodion has dried. The clamp is then removed and a condom is placed over the penis in order to protect the clothing in case the seal should break. The patient is instructed to avoid straining efforts which might cause the seal to break. This is repeated daily, as previously stated, until four urethral treatments have been administered. No other treatment is given except sulfanilamide orally, in 60 to 80 grain doses daily; after the second day the dosage of sulfanilamide is reduced by about one-third.

Usually the urethral discharge disappears and the urine becomes clear after the first treatment. If everything goes well sulfanilamide is discontinued after five days. After a lapse of one or two weeks without treatment a test with alcoholic beverages is permitted. If this fails to cause a flare-up, urethral sounds are passed and followed perhaps with an injection of 1 or 2 per cent silver nitrate solution. If there is still no recurrence of discharge and no gonococci are found, the patient is permitted to have sexual intercourse using a protecting condom. The semen is then examined for pus and gonococci and if negative after two such tests he is assumed to be free from gonococci.

We have treated seventy-nine consecutive patients by this method with but two failures. Although the sealing method for beginning gonorrhea has been used by us for a great many years, never were we able to obtain anything like such consistently good results before this treatment was supplemented with sulfanilamide.

Why is it that a local treatment of this kind can so greatly assist sulfanilamide in the treatment of early gonococcic infection? The answer is only problematical, but it may be because the organisms

lying on the mucosa or in shreds of mucus and pus are not reached by the sulfanilamide circulating in the blood stream.

A more or less analogous condition is seen in otitis media. The active inflammatory part of streptococcic infection in the middle ear responds well to sulfanilamide when the ear drum is incised, yet the organisms may be found in this area for a considerable time after all symptoms have subsided.

III. Sulfanilamide in Combination with Artificial Fever

So fascinating are the effects of the combined use of sulfanilamide and artificial fever that we almost begrudge the time already devoted to sulfanilamide. This combined treatment, however, is not employed for patients who make satisfactory progress with sulfanilamide alone, but for those who fail to respond or those, who, for domestic or business reasons, have urgent need for prompt cure of gonorrhea.

There appear to be adequate reasons for believing there are other resistant organisms which will respond as strikingly to this plan of treatment as do gonococci. Since our experience, however, with this combined use of sulfanilamide and artificial fever therapy has been limited largely to gonorrhea, we will devote the present part of the discussion solely to this infection, in which our results, in the treatment of obstinate cases, have far exceeded reasonable expectations.

Why are the results from the combination of sulfanilamide and artificial fever so much more spectacular than from either of these agencies when employed singly?

This is a hard question to answer except in a speculative way.

Among the things brought about by artificial fever alone, are:

1. Activation of tissue changes and stimulation of metabolic processes.
2. The pulse rate is increased about 16 beats for each degree of artificial fever.
3. The velocity of the blood flow is increased about 400 per cent when the oral temperature is 104 degrees.
4. The superficial blood vessels are greatly dilated.
5. The flow of lymph in the lymphatic vessels is probably increased.
6. The leukocytes and clasmatocytes are increased about 100 per cent.
7. The antibodies and other protective agencies are increased.
8. Of great significance from the standpoint of immunity is an immediate flare-up in syphilis of a weakly positive or negative Wassermann test to one strongly positive. This provocative action is due probably to the death of a large number of spirochetes.

These are facts already established by those who have studied hyperpyrexia. Fever acts like a call to arms. Body tissues, serum and cells, are placed on a warlike basis with defensive agencies mobilized and activated. This much is done by fever alone, and, when added to the advantages provided by the chemical attack on bacteria

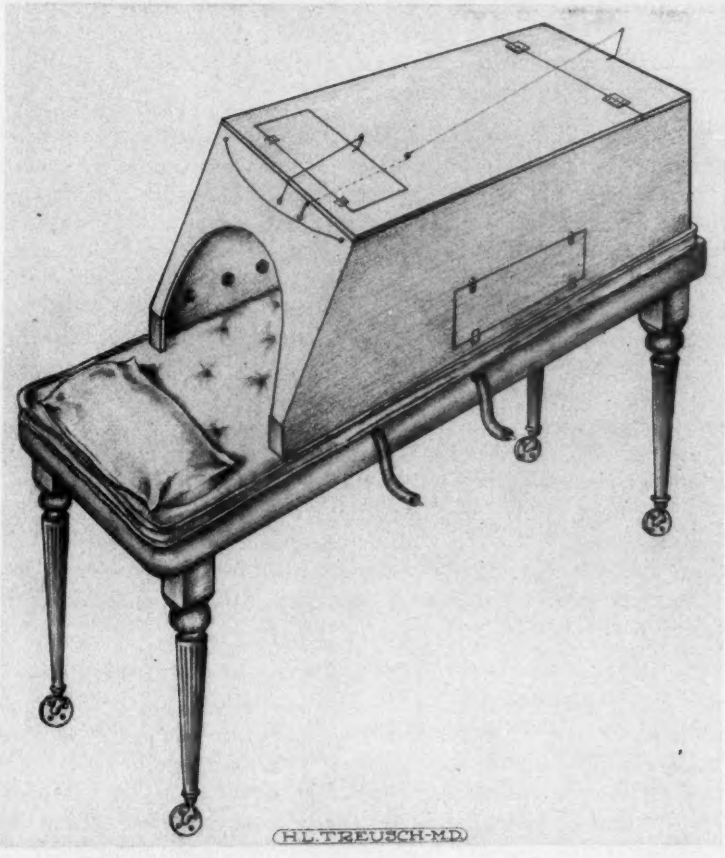

Fig. 1. Artificial fever cabinet. Note large space for neck and shoulders, and doors to be opened when cooling is desired.

with sulfanilamide, affords a combination analogous to a gas attack in a battle. Handicapped by the gas, enemy soldiers are more readily subdued by gunfire and bayonet.

There are still other things possibly induced or stimulated by artificial fever which may play a part in the beneficial effects of this agency in combating infection. Drinker, working on dogs, blocked

the lymphatics leading from the legs. The area with the lymphatics obstructed developed a surprising susceptibility to infection with streptococci—organisms which practically never infect dogs in their legs.

It is well known that the lymphatic system plays an important part in our own defense mechanism. Since blocking lymphatics lowers resistance against bacteria, it does not seem illogical to assume, conversely, that the stimulating effect of artificial fever might increase resistance against infection.

Fortunately, improvement in means for producing artificial fever came a little while before the advent of sulfanilamide. For a number of years we had been using artificial fever alone in the management of troublesome complications of gonorrhea. This was continued when sulfanilamide came into use. As far as we know, we were the first to combine artificial fever with sulfanilamide therapy. Soon we saw spectacular cures of stubborn, chronic cases which had been responding slowly or not at all to either of these or other agencies. Another pleasant surprise was that these patients were cured with the combination of smaller amounts of sulfanilamide and less fever than was ordinarily required. The danger of both these agencies was thus lessened and at the same time the comfort of the patient was increased. We soon found that a moderate amount of artificial fever, when employed with sulfanilamide, would cause urethral discharge to cease within twenty-four hours or less, and the urine to become clear within twenty-four to forty-eight hours. These results were obtained in about 90 per cent of the patients taking the treatment about to be outlined.

The artificial fever was usually administered every other day until three treatments were given. Sulfanilamide in doses of 60 to 80 grains was given daily for a day or so before the artificial fever treatment and continued during the intervals between them. It seems desirable for the patient to have a fair degree of tissue and blood concentration of sulfanilamide at the time of the fever treatments. It is preferable, however, for him not to have a disturbing amount of sulfanilamide. When disturbed by it, he may be less able to tolerate a satisfactory fever treatment. At the present time we have the feeling that 60 grains for two days before and during the intervals between the artificial fever treatments is sufficient. Whether sulfanilamide is continued after the fever treatment depends upon the circumstances. As a rule, it is better to know as soon as possible whether or not the treatment has resulted in the eradication of the infection. Such a rule, though, is not always advisable.

Preparation of Patients for Artificial Fever

Patients who would not be regarded as suitable subjects for major operations should not be given chemothermotherapy. The heart, lungs, kidneys and thyroid should receive especial attention in preparatory examinations. Since the flow of free hydrochloric in the stomach is checked by hyperpyrexia food should not be taken for several hours before nor for several hours after fever treatments.

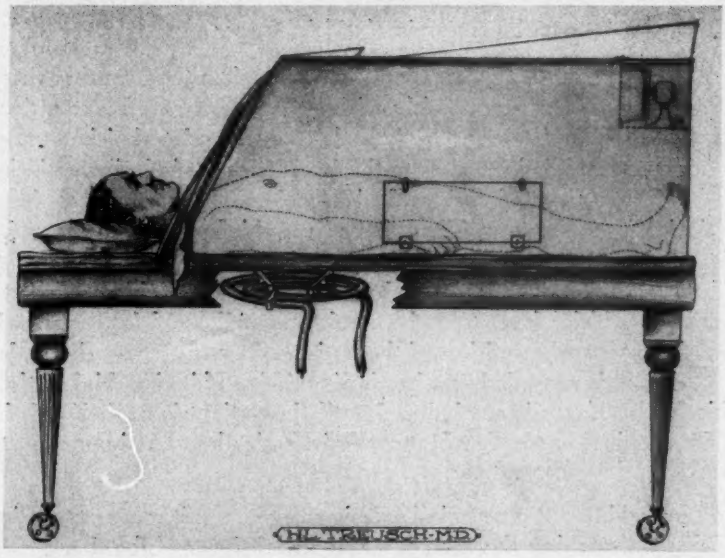

Fig. 2. Artificial fever cabinet, with patient in position. Note inductotherm coil beneath, and heating unit for cabinet and fan in separate compartment at upper part at foot. Fan blows warm air or cool air as needed.

Pantopon, ⅓ of a grain, by hypodermic is usually given as the fever begins to rise, or bromides may be given several hours before the treatment. Some patients prefer no sedatives. Breathing is sometimes difficult when the temperature reaches 101 or 102 degrees; sedation therefore with narcotics which slow the respiration should be avoided.

Stimulants as a rule are not needed, though hot coffee and tea may prove desirable. Heat stroke is an important thing to think of and means should always be at hand for administering oxygen, 95 per cent, and carbon dioxide, 5 per cent, by inhalation. Provisions for prompt cooling of the patient and adequate oxygen, with carbon dioxide, are probably the most important of all measures for emergencies which may occur during artificial fever treatments.

Since there is a great loss of sodium chloride through excessive sweating, this salt should be administered freely during the fever treatment. It may be given in capsules or tablets, or in water or grapefruit juice in 0.6 per cent solution. The patient is encouraged to take large quantities of such salines throughout the duration of the fever treatment. Calcium should be given if cramps occur in the legs or abdomen.

Dangers in Artificial Fever

Nothing said in this discussion should be taken to mean that these treatments can be given safely without constant careful attention. The doctors in charge as well as the nurses and technicians must be alert and well informed as to the modalities for inducing artificial fever. A number of serious accidents have been reported from artificial fever therapy. These have been chiefly from its misuse by those who were without experience or lacked adequate equipment. The greatest danger is from those who make a reckless effort to produce artificial fever to a given point regardless of danger signals or of the general condition of the patient. In our own work a pulse rate of 140 is regarded as a borderline limit. If it rises higher than this further fever is not induced until the patient is cooled and the pulse rate is slowed. Respiratory difficulty is almost as important to watch as the pulse rate.

Our cabinets are especially designed to permit prompt cooling without disturbing the set up for artificial fever. The doors may be opened and cool air blown on the patient as needed without disarranging the plans for continuing the treatment as soon as he feels sufficiently refreshed and reassured.

An effort is made to obtain an oral temperature of 103 or 104 degrees Fahrenheit for three or four hours. This effort is conditioned at all times by the manner in which the treatment is being tolerated by the patient.

After the treatment is over the patient is placed in bed for three to six hours or longer as required.

Unless contraindicated the artificial fever treatments for gonorrhea are given every other day until three have been administered. More should be given if the desired temperature has not been attained and maintained for three to four hours, or if the infection has not been exterminated.

Results Obtained by Treatment with Combination of Sulfanilamide and Artificial Fever

It is difficult to make an analysis of our results from the combination of sulfanilamide and artificial fever therapy because of the fact that for a considerable time we were feeling our way along with these two new and potent agencies. Safety was our watchword. We preferred to have the patients uncured than to take a chance with harmful results from the treatment.

As we had done with artificial fever alone for several years before combining it with sulfanilamide, we administered both to many patients as a palliative measure to reduce the pain resulting from a hyperacute epididymitis or prostatitis. Many of the patients were physically unfit for curative bouts of fever. Others had failed to respond to the usual measures of treatment.

A pulse rate of 140 was tentatively decided upon as a borderline of safety, and induction of fever was discontinued when the pulse reached this point. Being more or less arbitrary, this caused the fever treatment to be discontinued in many cases when it might have been carried higher and kept up with safety for a considerably longer time. Our percentage of good results, however, was satisfactory and we did not feel called upon to take unnecessary chances.

Thirty-one patients received what we regarded as fairly satisfactory bouts of fever and sulfanilamide therapy, both in amounts too small, when administered singly, to expect curative results. Of these thirty-one patients, twenty-four were cured promptly. By this we mean within a week's time or less.

Why the failures occurred we cannot say. Some who were cured received less adequate fever treatment than some who were not cured. We knew the organisms were resistant to the drug. If we had more time we would go into variations in the thermal death point of gonococci.

Among the complications in those who failed to be cured were, infected paraurethral follicles, prostatic abscesses and urethral strictures. One woman receiving what was thought to be adequate treatment, later showed gonococci in smears from the cervix.

Results so far, indicate that an oral temperature of 103 degrees for four hours or 104 degrees for three hours with the usual dosage of sulfanilamide will be curative about nine times out of ten when a fever treatment is given every other day until three treatments are administered if there are no "dead spaces."

"Dead spaces" in prostatic abscesses, in plugs of mucus in the cervix and in paraurethral follicles appear to be hindering factors and should be eliminated if feasible before the employment of chemothermotherapy. When this plan of treatment was used because of the urgency of domestic or business reasons, rather than because of resistant infection or complications, the percentage of cures with three fever treatments and sulfanilamide has been perfect.

Four patients with gonorrheal arthritis were quickly cured by this combined treatment; the painful symptoms disappeared within a few days. It took a longer time, of course, for the joints to limber up.

Four men and one woman were freed of gonococci by one treatment each. An equal number, however, failed to be cured by single treatments. The percentage of failures, therefore, is too high to recommend this procedure.

Summary

Sulfanilamide is the most valuable drug so far used in the management of many infections of the human body.

It has many disagreeable toxic manifestations, most of which disappear soon after the discontinuance of the drug. Not all of the toxic symptoms, however, require the cessation of sulfanilamide. The most dangerous, but uncommon, toxic reactions of this drug are on the red and white blood cells.

Clinical improvement from the use of sulfanilamide often far outruns the final eradication of infections such as those of the throat, middle ear, genito-urinary tract and uterus.

A very large percentage of immediate cures of beginning gonorrhea are obtained by supplementing sulfanilamide with the use of a 5 per cent solution of argyrol sealed in the anterior urethra where it is allowed to remain for four hours. This treatment is repeated once daily for four days.

With gonococcic infection, which has been resistant to sulfanilamide, most impressive results are obtained by the use of this drug in combination with artificial fever.

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OPERATIVE TREATMENT OF ESSENTIAL HYPERTENSION

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AMONG 386 operations on the adrenal-sympathetic system for essential hypertension we have performed 234 celiac ganglionectomies upon 141 patients.

The earlier operations which included adrenalectomy, and denervation of the adrenal glands with and without division of the major and minor splanchnic nerves were followed by immediate improvement but in six months or a year there was a recurrence of the disease due to the regeneration of the sympathetic fibers. Aided by studies in the comparative anatomy and physiology of the adrenal-sympathetic system, we came to appreciate the role of the sympathetic system in the mechanism by which oxygen is carried to the tissues, and therefore we carried our attack to that part of the sympathetic system which is most intimately concerned with this function, that is, to the celiac ganglion, the fibers of which, moreover, would not regenerate so that the results of celiac ganglionectomy should be more lasting than those of adrenal denervation or splanchnicectomy.

The immediate effects of celiac ganglionectomy are dramatic, the blood pressure often falling to or below the normal level during or immediately following the operation. The later effects upon the blood pressure have been almost equally dramatic in many cases. In 47.4 per cent of the patients the diastolic pressure was normal 7 to 12 months after the operation; in 15.8 per cent the blood pressure both systolic and diastolic was normal 7 to 12 months after the operation.

The effects of bilateral celiac ganglionectomy upon the blood pressure in a series of 69 cases is shown in the accompanying tables. In the 10 cases of unilateral celiac ganglionectomy in which we have results of over a year in duration the average drop in the blood pressure has been 26/13.

Even more striking than the effects upon the blood pressure has been the symptomatic relief of these patients. The general symptoms accompanying hypertension which were present when the patient entered the hospital were headache, nervousness, fatigue,

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palpitation, dizziness, excitability and irritability, precordial pain, and a sensation of tenseness.

A compilation of the data in our case histories has shown that complete relief in some cases, and in many cases marked relief from these symptoms have followed celiac ganglionectomy—relief from fatigue, headache, heart consciousness, dizziness, mental confusion. The eyesight has improved. Many patients have been able to return to their usual occupations even though the blood pressure has not been restored to the normal level. Even though the blood pressure has been reduced only from 280/150 to 180/120 or 200/135, the subjective improvement may be marked. Moreover, these patients tend to become calmer and more equable in temperament and thus even in cases in which the blood pressure remains well above the normal level the violent uprushes of the blood pressure with the disastrous results which may accompany emotional outbursts may be mitigated.

An analysis of the negative effects of celiac ganglionectomy also gives significant findings. Celiac ganglionectomy does not interfere with metabolism; it does not interfere with the digestive tract; it does not interfere with the genito-urinary tract; there are no orthostatic effects; there are no abnormal changes in the daily blood pressure; there are no changes in the skin; there has been no instance of adrenal insufficiency; there is no change in the rate of activity of the heart; there is no change in sex function.

In our series forty-eight patients complained of *headaches*. All were improved when they were discharged from the hospital, with complete relief of headaches in 14 per cent. During the first three months following the operation 87 per cent were improved, and of these 30 per cent were completely relieved from the headaches. During the four to six months postoperative period, of those from whom we have heard, 87 per cent were improved and 39 per cent were completely relieved. During the seven to twelve months postoperative period 100 per cent were improved and 42 per cent were completely relieved.

Thirty-six patients complained of *nervousness* when they entered the hospital. Ninety-four per cent were improved on discharge from the hospital and 16 per cent were completely relieved of nervousness. During the one to three month postoperative period 88 per cent were improved and 12 per cent were completely relieved; during the four to six months period 77 per cent were improved and 29 per cent were completely relieved; and during the seven to twelve months period 89 per cent were improved and 22 per cent were completely relieved of nervousness.

Twenty-eight patients complained of *palpitation* when they entered the hospital. On discharge from the hospital all were improved and 25 per cent were completely relieved. During the one to three, and four to six months postoperative periods, 90 per cent and 100 per cent respectively were improved, and 25 and 29 per cent respectively were completely relieved. None of the patients reporting during the seven to twelve months period made reference to the presence or absence of palpitation.

Similar improvement or cure was noted in the remaining subjective symptoms, such as chest pain, dizziness, heart consciousness, etc., which are characteristic of essential hypertension.

TABLE I

EFFECTS OF BILATERAL CELIAC GANGLIONECTOMY ON THE BLOOD PRESSURE

	No. of Cases	*Adm.*	*End of Period*	*Dif.*
In Hospital	69	220/130	169/111	—51/19
1-3 Mos. Post Op.	55	219/135	181/115	—38/20
4-6 Mos. Post Op.	33	236/138	191/118	—45/20
7-12 Mos. Post Op.	19	221/134	193/119	—28/15

The large majority of the patients operated upon for essential hypertension report a one to five year duration of symptoms. The duration of symptoms ranged, however, from one month to 25 years. Our studies have shown that the duration of symptoms has little effect upon the symptomatic results of celiac ganglionectomy.

Even in cases in which the blood pressure has been but little reduced the patients not only are symptomatically relieved but appear to be guarded against the violent uprushes of blood pressure which so often spell disaster for these patients with the malignant type of hypertension.

As to the criteria for operation our experience has shown that no absolute rule can be made. The decision in each case must be based upon the clinical judgment of the surgeon and upon the laboratory findings.

We have operated successfully in advanced cases of malignant hypertension, the degree of malignancy being judged by the extensive eye changes; we have operated successfully in the presence of glomerulonephritis, and upon patients who had had a cerebral hemorrhage.

In judging of the risk of operation in any individual case it should be borne in mind that the patient with essential hypertension especially in the malignant phase is a poor risk for any impact of life—for any type of fever, for pneumonia, for pregnancy, for muscular exertion, for emotional excitement; in other words, the risk of operation in cases of malignant hypertension is no greater than the risk of life itself. In our series of bilateral celiac ganglionectomies, it is interesting to note there have been only three deaths in the hospital from cerebral hemorrhage—a significant observation as far as the safety of the operation is concerned.

TABLE 2

REDUCTION OF BLOOD PRESSURE TO NORMAL AS RESULT OF BILATERAL CELIAC GANGLIONECTOMY

	On Disch. from Hosp.	*1-3 Mos. Post Op.*	*4-6 Mos. Post Op.*	*7-12 Mos. Post Op.*
No. of Cases.....	69	55	33	19
Completely Normal..	27.5%	18.2%	18.2%	15.8%
Blood Press. on Adm.	197/119	192/126	198/122	193/128
Diastolic Normal....	40.6%	41.8%	30.3%	47.4%
Blood Press. on Adm.	213/124	206/124	204/125	215/123
Systolic Normal.....	31.9%	18.2%	21.2%	15.8%
Blood Press. on Adm.	200/123	192/126	197/123	193/128

Since according to vital statistics 60 per cent of individuals with essential hypertension will sooner or later die of coronary disease; since in essential hypertension the heart has tremendous labor imposed upon it; because of the effort to circulate the blood against the high pressure, one might expect that heart failure would be one of the outstanding risks of the operation. In our entire series of cases not a death has resulted from heart failure. As soon as either the adrenal or the celiac ganglion is interfered with there is a fall in the blood pressure.

In 56.5 per cent of the cases in which bilateral celiac ganglionectomy was performed the blood urea was decreased, in 34.8 per cent to the normal level. Considering the general mortality from kidney failure and heart failure in cases of malignant hypertension the low operative mortality is far better than what one would expect. If in the presence of hypertension one is forced to operate on the gallbladder or on the stomach, the burden falls on the brain, the heart, and the kidneys, whereas, when celiac ganglionectomy is performed this burden is lessened and, therefore, it is logical to find a lower mortality from celiac ganglionectomy than from any other operation in the presence of malignant hypertension.

One point was made very clear by our experience and that was that when the kidney function is impaired there is very great danger in allowing the blood pressure to fall to too low a level. The blood pressure should be maintained at or above a certain level, say 90 systolic as a criterion.

Many suggestions have been made as to operability, many criticisms offered as to the analysis of end-results. As to operability as we have stated judgment is dependent in part, but only in part, upon the laboratory findings and principally upon the clinical experience of the surgeon. As to the end-results the final judge must be the patient himself. If he is relieved of his symptoms, and especially if he is able to return to his former occupation then the operation has been successful.

As for the life prolonging and palliative effects of the operation they have been as clearly demonstrated as have the effects of any operation for cancer. As for the more remote results we must wait until a longer time has elapsed.

AN EFFICIENT METHOD OF FIXATION AND IMMOBILIZATION OF UN-UNITED FRACTURES WHERE BONE GRAFTS ARE DESIRED

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MANY methods have been recommended in doing bone grafts, some of the most common of which are the inlay graft, the intramedullary graft, the osteoperiosteal graft and the onlay graft. It is not my purpose to go into what I believe are the merits of each of these methods, but it is my opinion that the most important factors to be considered are the complete fixation of the graft and the immobilization of the fragments. There are other considerations, of course, but they apply to any and every method used. For several years I have used the inlay graft, first, because I believe the blood supply is better and second, and more important, because the graft can be more firmly fixed in place by the method described.

Since bone grafts were first described, there has been a discussion, pro and con, of the material to be used in fixing the graft. Some years ago metal screws and nails were used extensively. They were later condemned in favor of the bone peg and the bone screw. It seems that at the present time a great many reputable surgeons like Gill[1], Key[2], and others, have returned to the use of metal screws. Campbell[3], who uses bone material in his fixations of bone graft, now uses metal in fixing numerous other fractures; this is true also of Speed[4]; Anderson[5] uses metal pins in his fixations of fractures as do Stuck[6] and many others. It seems to me that since metal is used so extensively by capable surgeons it is not so much a question of what is used as of how it is used. Probably the use of vitalium as described by Venable[7] will offer us a satisfactory metal for use in bone surgery.

My objections to bone screws and bone pegs are, first, no surgeon except one with highly trained assistants and a specialized working team of nurses can successfully use this technic. Second, one must be familiar with, and have access to, rather expensive and complicated instruments to do the work properly. Third, and most important, immobilization and fixation are difficult and usually inefficient.

My chief objections to metal screws are that, after a short time,

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due to absorption and softening around the screw, fixation is not complete; that the screws usually must be removed at a second operation, this being preferred in many cases to leaving a foreign body buried in the subcutaneous tissues. In many cases the screws may remain without doing harm but in others they set up an irritation or inflammation; immobilization is not complete even after the cast is applied for atrophy takes place and, as the cast loosens, the screws also become loosened and the fracture is left with only partial immobilization and fixation.

In doing a large amount of industrial surgery I have, of course, many cases of un-united fractures. In a number of cases it was impossible or inadvisable to send the patients away from home to some highly specialized clinic for a bone graft operation and especially when the results in a large percentage were not entirely satisfactory. It was for this reason that I tried to devise some operation that could be done by any capable surgeon without the use of highly specialized assistants and nurses and without the expensive and complicated bone instruments. It was also my purpose to find a method that would more nearly fix the graft and immobilize the fragments, at the same time making the patient ambulatory as soon as possible. After trying several different operations and studying the results obtained in many cases where various methods had been used, I decided that the two most important factors in a bone graft operation were the immobilization of the fragments and the fixation of the graft.

Such things as asepsis, blood supply, apposition of bone ends, removal of foreign material, interposed tissues and granulations between the bone ends are all important. Also the patient's general diet and general physical condition are important. It is especially important to treat such diseases as diabetes and syphilis, when they exist, before proceeding with any bone operation. Of course, it is not advisable to proceed with any form of bone graft in the presence of infection.

The method which I now use in a bone graft operation I believe to be simple, successful and without any serious objectionable features. This operation, to my knowledge, has never been described. I must admit, however, that I am indebted to the work of Roger Anderson for the idea as to immobilization of fragments and to Gill, Key and others for having returned to the use of metal for the fixation of grafts. The remainder of the procedure, I believe, is original.

The method used is this: the skin over the fracture is thoroughly sterilized. After ordinary precautions in draping the patient, a

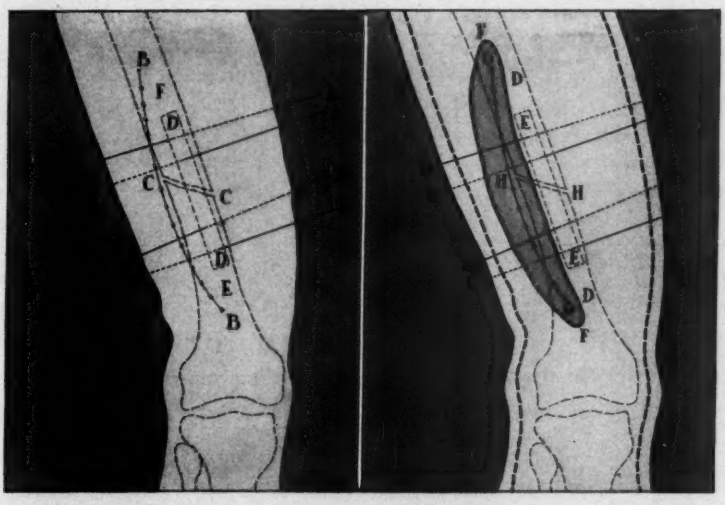

Fig. 1. A. Kirschner wires passing through skin, bone graft and upper and lower fragments at angles to each other. B. Skin incision is not directly over graft. Wires do not pass through the incision but do pass through the skin flap. C. Line of fracture. D. Bone graft (in-lay). E. Lower bone fragment. F. Upper bone fragment.

Fig. 2. A. Plaster cast. B. Kirschner wires incorporated in plaster cast but are not parallel to each other. C. Kirschner wires incorporated in plaster cast but are not parallel to each other. D. Upper and lower fragments of fractured bone inclosed in cast. E. Bone graft (in-lay). F. Window cut in cast allowing free access to incision G but not interfering with wires B and C. Wires C do not pass in region of window. H. Line of fracture.

These diagrams show fracture of a single bone because it is easier to demonstrate the procedure used.

curved incision is made varying in length according to the fracture and the extent of displacement. It is very important to make the incision so that the line of incision will not be directly over the bone graft, (fig. 1) because, first, there is less chance of infection, especially if serum accumulates under the skin; second, I believe the blood supply will be better if the graft is under a flap of the skin rather than under a direct line of incision; third, and most important, a window can be cut in the cast over the incision without disturbing the remainder of the operation; and fourth, the wires used in the operation, which I will describe, must be incorporated in the cast and away from the window.

After dissecting back the skin flap, the end of the bone fragments are curetted and all foreign and interposed material removed. The ends of the bone are then approximated end to end, if possible, and held in place with bone clamps. The next step in the operation is to chisel out a large enough inlay graft to take care of the fracture involved. This can be done in a manner similar to any technic in

getting the graft. I use a sharp chisel instead of an electric saw because it is simpler, more convenient and without so much cumbersome equipment. Also, I believe that the chiseled graft can be made to fit in place much better. After the graft is placed I then insert through the skin flap a Kirschner wire, which is drilled through the graft and through the bone fragment. Usually two pins in the upper fragment and two in the lower fragment (fig. 1) are sufficient. Sometimes an additional pin below and one above, not in the graft, but in the bone proper, are used in order to secure more stable immobilization. The wires are inserted at angles so they will not be parallel to each other in order to make immobilization and fixation more effective (fig. 1). The bone clamps are now

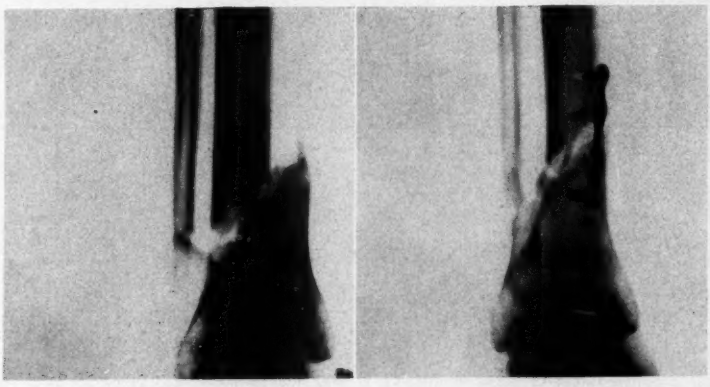

Fig. 3. Original fracture after two attempts to hold it in place after perfect reduction.
Fig. 4. Perfect reduction. Bone plate applied showing loosening of screws due to absorption around them.

removed and the wound sutured without drainage or, in some cases, a small drain is inserted in either end of the incision extending just below the skin.

The wound is dressed and a plaster cast applied, incorporating the ends of the four Kirschner wires (fig. 2) and in most cases the joints above and below the fracture. The protruding ends of the wires are then filed off and a window cut in the cast (fig. 2). If it seems advisable the cast can be split without interfering with immobilization and fixation. The patient can be made ambulatory in a few days following the operation. The cast is usually removed in from six to eight weeks, if desired, and the wires are slipped out without further operation, being careful, of course, that the field through which the wires are pulled is well sterilized. If further immobilization is necessary another cast or a walking boot can be applied.

Probably it will be of interest and make the procedure clearer if I present the following case:

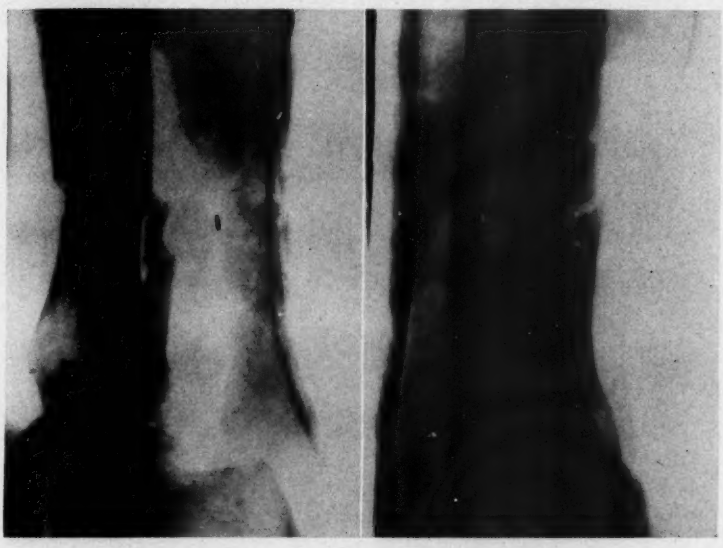

Fig. 5. Bone plate removed. Leg put in walking cast.

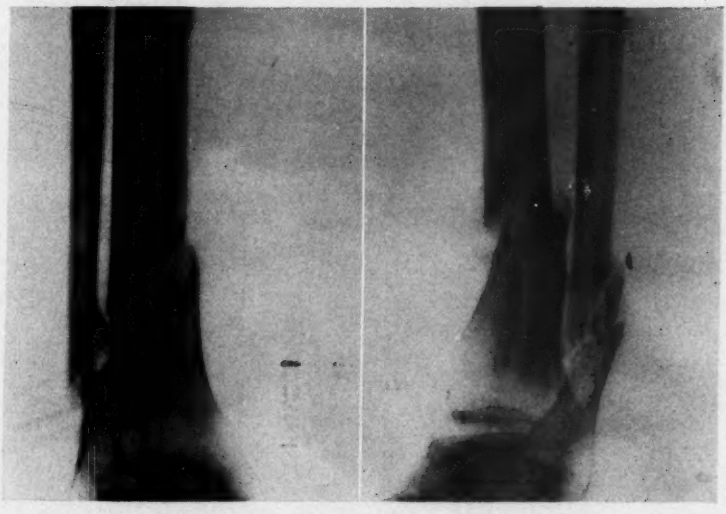

Fig. 6. View of leg in walking brace, showing non-union.

Mr. L. S., aged 37, was brought in to the Jackson Infirmary with a fracture of the right leg just above the ankle. The history otherwise was irrelevant. Physical examination was negative except for the fractured leg.

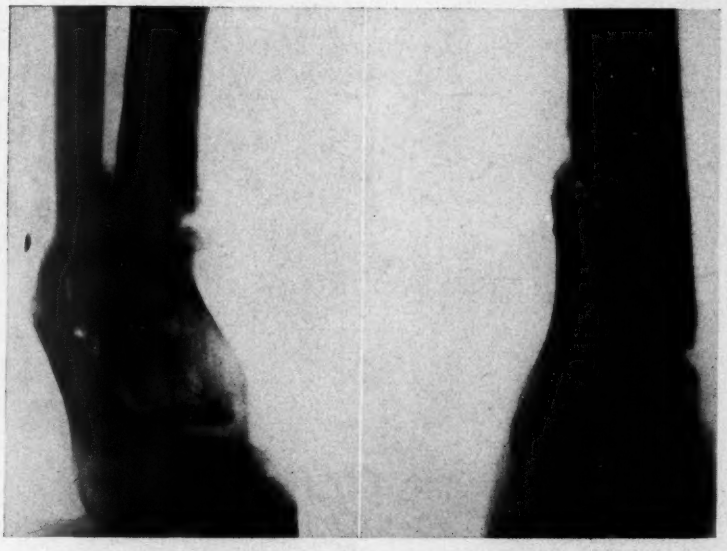

Fig. 7. Progressive backward bowing of fragments.

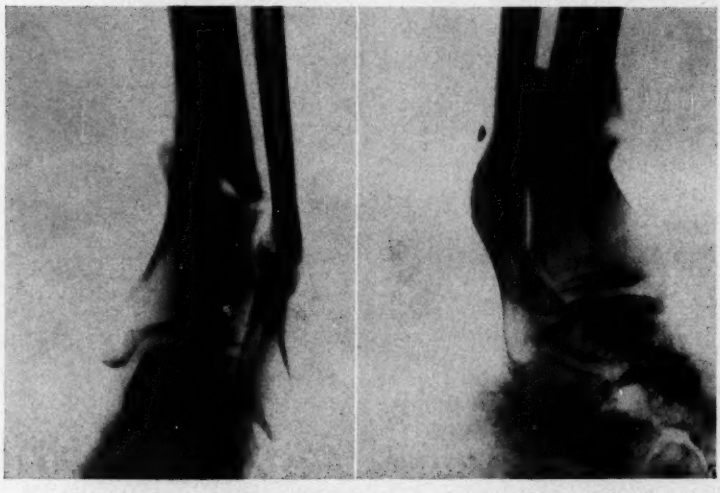

Fig. 8. Un-united fracture with further bowing backward of fragments. This series shows the impossibility of immobilizing the un-united fragments by cast alone.

After setting the fracture perfectly under the fluoroscope on two occasions it was found impossible to hold the fragments in place (fig. 3). The bone was plated as shown in figure 4. In this illustration also can be seen the rarefied area around the short metal screws which prevented complete fixation. After

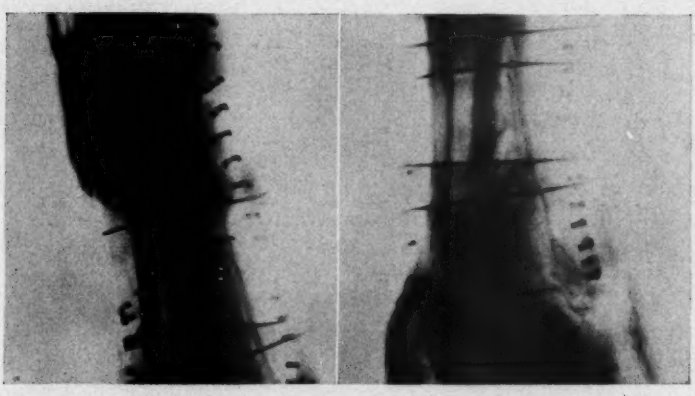

Fig. 9. Kirschner wires in place, bone graft in place, ends have been cut off even with surface of cast. A window has been cut in cast, also shows line of incision.

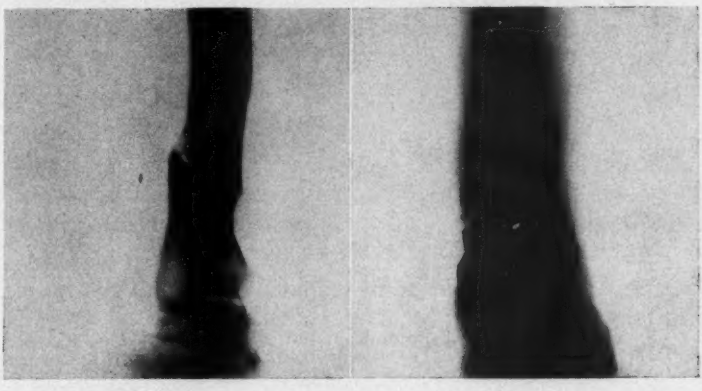

Fig. 10. Good callus formation. Strong union and good functional results.

six weeks the plate was removed (fig. 5) and the leg placed in a perfectly fitted walking plaster cast. Union still did not take place and backward bowing of the fragments was progressing as is seen in figures 6, 7 and 8. These illustrations also show the rarefied area where the metal screws had been removed and only partial immobilization was obtained. About eight months after the original fracture a bone graft was done by the method which I have described (figs. 1, 2, and 9). These figures also show the bone graft in place, the Kirschner wires in place and the area of the skin incision. Also the window which was cut in the cast. This cast was left on for eight weeks when it was removed, the wires being removed at the same time. The skin clips had been removed on the seventh day through the window in the cast.

An efficient walking leather boot was molded and tailor made for the leg. This boot was worn by the patient for about four months and then discarded.

At the present time the patient is walking without any support. The fracture shows firm union and is in good position (fig. 10).

Conclusions

It is my opinion, after using all ordinary and accepted precautions, that

The most important principles in bone grafts are immobilization of the fragments and fixation of the graft.

The inlay graft is best suited to the operation described.

By using through and through Kirschner wires immobilization and fixation can best be accomplished.

This method of immobilization is especially good as the leg atrophies, becoming smaller from disuse, causing the cast to loosen.

Even if absorption takes place around the wires, fixation and immobilization remain efficient.

Short screws or pegs of any material neither fix the graft securely nor immobilize the fragments completely.

The patient can be made ambulatory in a very short time, which tends to make him more comfortable, favors callus formation and, not of least importance, lessens the hospital expense.

No infection has occurred in any of my cases and I believe that infection following this type of operation is of no greater incidence than in any open bone operation.

The method can be used by any capable surgeon in any hospital with perfect safety and with good final results.

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ALLERGY:
ITS RELATION TO THE SURGICAL SPECIALTIES

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BY clinical experimentation and actual pathologic findings, allergic phenomena have been raised from the depths of medical conjecture and established as facts. It has been shown that these phenomena may occur in all the anatomic systems of the body and that allergic causes must be considered in the study of any altered physiology.

Time does not permit a discussion of the mechanism of allergic reactions and the resultant changes, but we request that you keep in mind the chief components of the allergic reaction:

1. Smooth muscle spasm.
2. Increased capillary permeability, resulting in
3. Cellular infiltration and edema.

Remember also the altered physiology that may be the result of the above-named reactions occurring in the various tissues of the body. Smooth muscle spasm occurring in a hollow viscus, such as the colon or ureter, would result in pain; in the arteries of the extremities, pain; in the arteries of the brain, reduced blood supply; in the lungs, asthma. Cellular infiltration and edema would result in nodular infiltration about the blood vessels, with altered blood supply, increased pressure, localized and general, in the skull cap and along nerve sheaths, the actual closing of vessels, and the destruction of tissue.

Allergic reactions may occur suddenly or slowly, may disappear suddenly, or may last for an indefinite period. These reactions may be reversible or irreversible, but reversible reactions recurring in the same tissue frequently or for a continued period of time may in the end produce permanent tissue changes.

We shall discuss briefly the allergic reactions that must be considered by the various surgical specialties, but only those reactions which *have proven* to be at times due to allergy.

THE NERVOUS SYSTEM

The most interesting of the allergic reactions affecting the nervous system have been called "cerebral allergy". The chief symptoms are

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nervousness, headache, vertigo, mental confusion, inability to control speech, numbness, tingling, transient paralyses, and occasionally unconsciousness with or without epileptiform convulsions. Some of these cases are typical of hysteria and others simulate the symptoms produced by brain tumor or epilepsy.

From our cases we have selected three examples:

CASE 1. Our first case was that of a doctor's daughter, 16 years of age, away at school. She complained of attacks of mental confusion, a sort of mirror-speech she described as "saying things backwards," vertigo, headache, nausea, and numbness of parts of the body. These attacks came on in class.

Our diagnosis from her history of the present illness was hysteria. Neurologic examination was negative.

There was a family history of allergy, and the patient herself had suffered from other forms of allergy. Skin tests gave markedly positive reactions to certain foods, to pollens and to other inhalants. Appropriate allergic treatment relieved the symptoms.

CASE 2. A lawyer, 37 years of age, complained of attacks of vertigo, headache, mental confusion, inability to control words, and, at times, unconsciousness and epileptiform attacks. During these attacks, if he tried to say, for instance, "Here comes Mr. Smith," he would quite likely say, "Yonder goes Mr. Brown." He was obliged to lie down whenever and wherever these attacks occurred. The main causes of his attacks were found to be eggs and shellfish. These were removed from his diet with resulting relief.

CASE 3. An 18 year old student at one of the local preparatory schools fell unconscious on the football field, and was thought to have suffered from concussion caused by a blow on the head. Later, he had a similar attack without the possibility of injury. There was a family history of allergy, and skin tests were positive for several foods.

Before his case was finished, he had another attack in a neighboring city, where a diagnosis of brain tumor was made. The doctor called us, and we advised the administration of epinephrine and calcium chloride intravenously, which relieved the attack. Appropriate allergic treatment was effective in this case.

Henry,[1] of Memphis, reports one case of allergic migraine explored by a brain surgeon for tumor, and two cases of headache in children, on whom ventriculograms were made for suspected brain tumor. All three patients were allergic, and their attacks were relieved by diet.

Convulsions in young babies have been shown to be caused by foods, chiefly milk, eggs, and cereals.[2] Allergic reactions have been shown to be responsible for some cases of paralysis, neuralgia, polyneuritis, blindness, delirium, unconsciousness, migraine, epilepsy, and psychic changes.[14, 15, 16, 17, 18, 19, 20] Epilepsy is usually caused by foods, but may be caused by inhalants.[21, 22, 23, 24]

The Ocular System

Among the allergic manifestations encountered by oculists are vernal catarrh[4,5] and acute or chronic conjunctivitis,[7,8,9,10,11] unilateral or bilateral. Some chronic cases of allergic conjunctivitis have been mistaken for trachoma or phlyctenular conjunctivitis. Fort[4] first reported a case of vernal catarrh caused by pollen.

In some cases there is seen a very marked pericorneal injection, with itching and photophobia. There has been reported one case of left macular edema occurring with gastrointestinal allergy and eczema, caused by food.[12] This condition disappeared when the food was omitted from the diet, and returned when the food was experimentally eaten again.

Other lesions in the eye shown to be due to allergic reactions are retinal edema, with or without hemorrhage, and edema of the optic disc.[13] Balyeat and Rinkel[6] reported a case of episcleritis recurring with hay fever every four or five months for 12 years, relieved by allergic treatment.

A syndrome called "eye allergy", consisting of conjunctivitis, at times with a combination of other symptoms such as eczema, urticaria, and angioneurotic edema of the lids and skin about the eyes, frequently appears to be due to contact allergy. We have had several patients, some of whom gave positive reactions to intradermal tests and some to patch tests.

Endophthalmitis phaco-anaphylactica is a severe reaction seen in eyes in which lens material has been left after cataract extraction, and in children after the second discission for cataract.[3]

Corneal ulcers have been shown to be due to sensitivity to foods and to inhalants.[44] Rowe describes the case of a boy with corneal ulcer due to eating chocolate, duration eight months.[21] Other corneal ulcers and dermatitites about the eye, or conjunctivitis, may be due to contact allergy, to hair dye or "lash-lure".[45,46,47,48]

The Respiratory Tract

Nose and Sinuses: During the last few years, the attitude of the surgeon toward allergic conditions of the nose and sinuses has changed. Hansel[25] in his book, *Allergy of the Nose and Paranasal Sinuses,* gives an excellent resume of the experimental work and clinical observations by the profession which have brought about a formulation of the present ideas. Surgeons are now slow to operate in the presence of allergic conditions affecting the nose and sinuses until allergic treatment has been instituted. Operations neither relieve nor cure allergy. However, obstructing polyps should be

removed, pressure from deflected septums relieved, and infection in the sinuses cared for just as if allergy were not present. Operations are best performed between the acute allergic attacks.

A definite effort should always be made to differentiate between allergic and non-allergic conditions of the nose and sinuses.[29, 30, 32, 35, 36, 37, 38, 39, 40] In general, a history of other allergic disturbances in the family or in the patient should make one suspect that an allergic reaction is causing the condition in the nose. The presence of edema of the nasal mucosa and of eosinophils in the secretion is almost pathognomic of allergy. Hansel states that 75 per cent of the cases of nasal allergy have other symptoms of allergy. It must not be forgotten that foods as well as inhalants may be the cause of nasal allergy. Eyermann reported 95 cases in which symptoms could be produced by the ingestion of foods, the most important of which were wheat, eggs, milk, chocolate, white potatoes, and string beans.[41, 42, 43]

Some rhinologists believe that all edematous polyps, either in the nose or in the sinuses, are allergic in origin.[26, 27, 28, 29, 30, 31, 32, 33, 34] Pathologic examination has shown the presence of eosinophils and of Charcot-Leyden crystals in a large percentage of such polyps.

Hansel, Alexander and others have concluded that ionization of the nasal mucosa is indicated in certain cases of vasomotor rhinitis in which no sensitization can be found.[25, 81, 82, 83] Alexander advises that one side of the nose at a time be ionized. Ionization is not indicated in ordinary pollen hay fever.

Pathologic and physiologic examinations have shown that the immediate effect on the tissues in the nose from ionization is an acute inflammation, and that the process subsides in from ten to fourteen days. In some cases, the tissues return to normal, but in others the ciliated epithelium is destroyed. In still other cases fibrous changes take place and these result in permanent damage to the tissues; in a few there follows a suppurative sinusitis with loss of sense of smell.

Alexander found that cases of pollen hay fever ionized before the season as a prophylactic measure did not do well. If the ionization was performed during the pollinating season, the success of the treatment depended upon the duration of the season after the treatment. Alexander and Parlato have both reported cases of asthma complicating hay fever, occurring for the first time after ionization.

Allergic angioneurotic edema of the larynx occurs, and is at times responsible for sudden death.[25, 49, 50, 51] Most of these cases occurred after the administration of serum or following insect bites.[56, 57, 58]

We have just seen a case of marked generalized urticaria with difficulty in breathing and speaking in a child 10 years of age, following a wasp-sting.

The administration of iodized oil is of great assistance in the treatment of some cases of asthma.[52, 53, 54, 55] Its use is indicated in any case of asthma which is unrelieved by other treatment, and especially in cases complicated by the presence of subacute or chronic bronchitis or by bronchiectasis. The oil is not broken down in the lungs, no iodine is liberated, and its action is purely mechanical. It acts by loosening viscid secretions and displacing them upward, allowing them to be coughed up more easily, and by the same method assists in the relief of infection. Atelectatic areas in asthmatic lungs have been opened up by the use of this oil. The less viscid oil of lighter gravity is used in cases of acute asthma and the heavier oil in cases of bronchiectasis. The oil may be administered by means of the bronchoscope, but there are much simpler methods of administration, for which we refer you to the literature on the subject.

Contraindications for the use of iodized oil are as follows:

1. Fever or cachexia.
2. Active pulmonary tuberculosis.
3. Congestive heart failure.
4. Sensitivity to iodine.
5. Sensitivity to the oil base.

Iodized oil should never be administered until the operator is sure that the patient is not sensitive to the oil or to the iodine. Patients usually know if they can take iodides. They should be skin tested for sensitivity to the oil base used. Poppy seed oil, peanut oil, and oil of sesame are the three mediums most commonly used. Several violent reactions have been reported due to sensitivity to the oil.[21, 60]

Bronchoscopy: In certain cases of asthma not yielding to treatment, the bronchoscope has been used for diagnosis, and has shown that the symptoms were due to foreign bodies, tumors, infections, or to pressure on the bronchi from external bodies. In other cases, the bronchoscope has been used to aspirate the thick, tenacious secretions, and some patients have been given relief for long periods. In still others, the bronchoscope has been used to open up atelectatic areas caused by the secretions mentioned above. Culture-material for making autogenous vaccines is sometimes obtained through the bronchoscope.[71, 72, 73, 74, 75, 76, 77, 78, 79, 80]

Tonsillectomy: The removal of the tonsils does not help asthma. Some patients are relieved for a short time after operation, others

have an increase of symptoms, and some are not affected.[12, 43, 62] Many patients give a history of asthma or of nasal symptoms beginning shortly after the removal of the adenoids and tonsils.

The Ears: Eczema of the external auditory canals is sometimes allergic in origin, and does not yield to the usual treatment.[25]

Typical symptoms of Menière's disease, usually deafness, vertigo, and tinnitus, have been proven to be due to sensitization to both foods and inhalants, frequently to house dust and orris root.[61, 63, 64, 65, 66, 67, 68, 69] One woman had suffered from such attacks recurring over a period of fourteen years; she was relieved only by the removal of orris root from her environment.[70] The attacks usually appear suddenly, and, if severe, there are often also nausea, vomiting, and a spontaneous nystagmus. Epinephrine will relieve some attacks.

The Gastrointestinal System

Acute Appendicitis: Allergic reactions not infrequently cause acute attacks of abdominal pain simulating diseases of the stomach, gallbladder, appendix, or large or small intestine.[64, 84, 85, 86, 87, 88, 89, 92] The pain is often localized over the region of the appendix, and may be accompanied by nausea, vomiting, rigidity, and fever.[90, 91] Unfortunately, either a leukopenia or a leukocytosis may occur, with or without eosinophilia. Henry reports three cases of operation for acute appendicitis in all of which edema of the intestinal walls was found but no special disease of the appendix. These cases were proved to be allergic. In three cases of our own, operation for acute appendicitis revealed edema of the ileum and free fluid in the abdominal cavity. One of these patients had a strong family history of allergy, but allergy was not suspected as cause for the symptoms at the time, and the case was not followed. Rowe[21] states that of 270 appendectomies done in cases of gastrointestinal allergy, 107 of the patients were not relieved of their symptoms by the operation.

There is as yet no accurate method of differential diagnosis between this condition and acute appendicitis, so the surgeon must continue to operate in doubtful cases.

Intestinal obstruction: Other cases with urticarial or angioneurotic lesions of the intestinal wall duplicate the symptomatic picture of intestinal obstruction. A doctor of our acquaintance was himself opened up for this condition. He had a very marked food allergy.

Cardiospasm and pylorospasm: Cases of marked cardiospasm or pylorospasm from sensitivity to foods have been seen in adults.[59] Many cases of allergic pylorospasm in infants simulate pyloric stenosis, and are relieved by diet. Cohen and Breitbart[93] state that the

pathology of infantile pyloric obstruction may be identical with that of allergy, that other evidences of allergy are present in the majority of cases of infantile pyloric obstruction, that these infants later in life develop eczema, urticaria, gastrointestinal symptoms, headache, asthma, or nasal allergy; and that pylorospasm occurs in allergic patients with or without organic obstruction, depending upon the time of life at which sensitization occurs, and upon the frequency and the severity of the shock reaction.

Peptic ulcer: Allergic reactions frequently cause typical symptoms of peptic ulcer, usually of the duodenal type, with or without the presence of actual ulceration.[21, 59, 94, 95, 96, 97] Ulcers which tend to recur after operation should always be investigated from the allergic standpoint. Ulcer patients who do not improve on the Sippy diet may be sensitive to milk.

Gallbladder and Liver Syndrome: Attacks caused by food allergy at times simulate acute biliary colic, but more often give the symptoms of chronic indigestion with pain in the right upper quadrant, with or without jaundice, simulating a chronic cholecystitis.[21, 59] Jaundice in such cases is probably due to an obstructive edema of the bile ducts, but may be due to vascular lesions.

Pruritus ani: Many cases of pruritus ani have been found to be due to food sensitivity.[21, 99, 100] One case, that of a doctor, was caused by eating chocolate. In addition to the pruritus, there is at times a perianal infiltration with cracking and oozing of the skin.

Proctitis: Rowe[21] mentions several cases of allergic proctitis. Patients awoke early in the morning with tenesmus, expulsion of mucus, blood, and gas. Other reports appear in the literature.[98]

The Genito-Urinary System

Recurring attacks of frequent and painful urination without demonstrable lesion, and finally proved to be due to sensitivity to foods, first called attention to allergic reactions in the genito-urinary tract.[21, 101, 102] We have seen several such patients, most of whom gave reactions to eggs, wheat, or milk, and one patient who gave positive reactions and positive leukopenic indices to several different foods.

There occur also allergic spasms in the ureter, sometimes so near the kidney pelvis as to be diagnosed kidney colic from stone. Hemorrhages from the bladder or kidneys and polyposis in the bladder may be due to allergy. Hematuria with a severe and possibly fatal nephritis may occur, together with urticaria, angioneurotic edema, purpura, and swelling of the joints.

Briggs reported a case of fulminating edema of the pelvic organs

which was diagnosed as ruptured tubal pregnancy and operated on.[104] Davis reported a case of pain in the prostate and seminal vesicles occurring in a patient always simultaneously with hay fever.[103] We are now testing a patient (referred by a urologist) who complains only of pain in the prostate of two years' duration. Skin reactions have been positive to several foods. This case will be reported later.

Several cases of intermittent bearing-down pains in the vagina and at times one of the vulva have been relieved by diet.[21] Cases of burning, itching, eczematous eruption, and edema about the vulva and vagina have been due to allergy and relieved by diet. Proven allergic symptoms associated with the uterus are painful, scanty, excessive, or irregular menstruation and leukorrhea.[111]

During pregnancy, attacks of asthma may begin, or may be increased, but more often they are relieved during pregnancy, to start again later. There is no contraindication for allergic treatment during pregnancy, if care is taken to prevent the constitutional reactions that might be caused by the injection of too massive doses of extract.[12]

Uterine spasm has been shown in one case to be due to pollen extract injections, and in another to be due to contact with orris root.[112]

Bones, Joints, Tendons

Arthritis: Swelling, redness, and pain about the joints occur often in allergic individuals, and are usually due to foods or to the injection of serum.[108, 110] There has been reported one case of arthritis caused by the inhalation of spores of fungi.[21] Any joint, any combination of joints, or even all joints may be involved. In involvement of the mandibulomaxillary joint, the condition must be differentiated from tetanus. Allergic arthritis occurs at times with urticaria, angioneurotic edema, purpura, and hemorrhagic nephritis.

The relation of bacterial allergy to joint disease, and the relation of allergy to atrophic and so-called infectious arthritis, have not been proved, but certain articles in the literature on bacterial allergy suggests that this type of arthritis is due to bacterial allergy, at least in certain cases.[105, 106, 107, 109]

Fibrositis: Fibrositis due to allergy is quite often seen, usually caused by foods.[116] Symptoms vary from slight pains in the muscles to very severe pain along the tendon sheaths. In one case we have observed a friction rub which could easily be heard upon motion of various muscles of the forearm or leg.

Hydrarthrosis: Hydrarthrosis has been proven to be allergic in

some patients, occurring after the injection of serum or after the eating of certain foods.[21, 117]

Blood Transfusions

Anaphylactic shock and sudden death have occurred in allergic individuals during or following blood transfusions.[113, 148] This is supposed to be due to the fact that proteids may pass into the blood unchanged by digestion.[115] For this reason, many doctors now recommend starving a donor from three to twenty-four hours, if the patient is allergic or has a family history of allergy.[114] In any event, the patient must be watched closely, the transfusion stopped at once if any untoward symptoms develop, and large doses of epinephrine administered subcutaneously, or, if necessary, intravenously, one minim or more per minute.

Catgut Sensitivity

Sensitivity to catgut has in some cases apparently been responsible for premature absorption of the gut, opening of the wound, and even postoperative hemorrhage.[124, 125, 126] Sensitivity to catgut may be sensitivity to sheep, as most catgut is made from sheep intestines. Rowe reports a case of generalized dermatitis in a surgical patient, occurring during convalescence and proved to be due to the formaldehyde in the catgut.[21]

Ether and Ether Anesthesia

Duke and Waldbott have recorded cases of asthma and nasal allergy due to ether sensitization. This evidently occurs very seldom.[119, 120, 123]

Ether anesthesia has been extensively used for the relief of status asthmaticus, of intractable asthma, and even in chronic asthma of moderate severity. Kahn advises gas-induced deep surgical ether inhalation anesthesia for ten minutes.[122] For rectal administration Maytum advises 30 c.c. of 50 per cent ether in olive oil for each twenty pounds of patient's body weight.[121] Asthmatic attacks may be relieved for several months in this manner. The anesthesia may account for the relief of asthma following so many different operations, for which relief the operation and not the anesthetic has received credit.

Endocrine Products

Allergic reactions have been reported occurring after the administration of many endocrine preparations, both the powdered ex-

tracts and the liquid hormones.[21] These reactions have varied from an itching skin rash with slight discomfort to the occurrence of a constitutional reaction with severe asthma, urticaria, angioneurotic edema, and shock. Reactions have been seen following the ingestion of extracts of thyroid, pancreatin, trypsin, and liver, the injection of insulin, epinephrine, pituitrin, the pituitary-like hormone,[132] and estrogenic substance. Allergic reactions to insulin often develop after it has been used for a period of one to three weeks, and may consist of any combination of the following: Itching, erythema, urticaria, angioneurotic edema, spasm in the gastrointestinal tract, vomiting, and diarrhea.[127, 128, 129, 130, 131] Some cases have reacted to all makes of insulin, but others may be able to take one product without trouble, and not another. This is true of all the extracts and hormones, since a patient may be sensitive to a preparation from beef and not to that from pork or sheep, or the converse.

Forman reports some cases of vasomotor rhinitis with hypothyroidism, relieved by the administration of thyroid extract.[118] We ourselves have many cases of urticaria, angioneurotic edema, and a few cases of asthma in women, which have been greatly relieved by the administration of estrogenic hormone.

Arthus' Phenomenon

There have been reported reactions like the phenomenon of Arthus, with sloughing of the tissues after the injection of serum.[144, 146, 147] In the case of a child given an injection of toxin-antitoxin, this sloughing reaction began on the buttocks and extended down the leg and upward into the abdomen, finally causing death.[145]

Radium

In allergic individuals in whom nasal polyps continue to recur after following the best recognized allergic treatment, the use of radium has been advised.[25, 134, 135, 136, 137, 138, 139, 140] Radium has also been used in cases of nasal allergy without polyps, with excellent results.[141, 142, 143] Hansel emphasizes that radium should not be used if the treatment by allergic methods is successful.

Drug Sensitivity

It is hardly necessary to mention the various and well known reactions from the injection of bismuth, iodine, mercury, arsenic, and the like.

We must not overlook the contact dermatitis from local anesthetics, which develops on the hands of surgeons, especially of eye, ear, nose and throat specialists who use them constantly.

It is not unusual to find patients showing a contact dermatitis from adhesive tape.

Infusions of acacia are occasionally administered intravenously for surgical shock. One patient who received acacia in an enema developed nasal obstruction, lacrimation, and laryngeal stridor.[133] If this patient had received it intravenously for shock, the result would hardly have been pleasant.

Conclusion

The importance of allergic phenomena in the field of surgery is based, not upon the frequency of their occurrence, but on the rarity with which they are recognized.

In atypical cases, in patients who do not respond to the accepted treatment, and in patients who have a history of allergic disturbances, either in themselves or in their families, allergy should be suspected as a cause of symptoms, and the case investigated from this approach.

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EDITOR'S NOTE—Lack of space prevents the publication of the complete bibliography. It will appear in the authors' reprints.

DEODORIZATION AND MANAGEMENT OF FUNGATING WOUNDS IN MALIGNANT DISEASE

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SLOUGHING fungating lesions in advanced cases of malignancy are equally trying to the physician and to the patient. Even when the tumor ultimately responds to surgery or irradiation there is a prolonged period in which the foul odor and continuous discharge of the wound prevents the patient from mingling freely with friends or family. The management of such cases should aim not only at the ultimate healing of the wound, with eradication of the disease when possible, but should also include attempts to cleanse, deodorize and disinfect the lesion. In the cases about to be described the use of an organic chlorine antiseptic in the form of azochloramid has proved of value in treatment.

CASE 1.—The patient was a white woman, aged 32. A little over three years before a small nodule had appeared on the right thigh and bled on several occasions. The lesion was excised with an electric cautery. Microscopic examination showed a malignant pigmented mole. An excision of the entire area was performed and the inguinal lymph nodes were resected. This was in the fall of 1932. There was no further trouble until November, 1935, when the scar, which had been gradually thickening, showed pink elevated areas. These areas on microscopic study showed recurrence of the original growth. Following a second excision in January, 1936, there was local recurrence, as well as recurrence in the inguinal region, progressing rapidly. The right leg became swollen and painful, due to the venous blockage, and the recurrence at the site of the scars broke down and ulcerated.

Figure 1 shows the condition of the leg at the time of admission to the hospital in April, 1936, and Figure 2 the microscopic structure of the tumor. In the next two months, although irradiation was given, the tumor continued to spread over the surface of the thigh and to extend beneath Poupart's ligament into the abdominal cavity. In spite of the rapid increase in size of the masses above and below Poupart's ligament, the patient remained free of any signs of distant metastases but suffered from pain and discomfort produced by mechanical pressure of the tumor on the vessels of the leg and the intrapelvic organs.

More discouraging and disheartening to the patient than pain, which was relieved by doses of morphia at four-hour intervals, was the foul odor and the incessant weeping of the lesion. The odor was sufficient to fill the entire room. The patient who had always been meticulous in regard to her personal appearance, was aware of the odor and greatly depressed by it: she considered

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it the chief cause of her loss of appetite. Numerous deodorants had been tried without effect.

While the patient was being given irradiation in the spring of 1936, she was put on the following regime. She was advised to get into a tub of warm water and allow the leg including the surface of the wound to soak for fifteen

Fig. 1. Large melanosarcoma of the thigh recurrent after two excisions, before the onset of deep x-ray therapy and azochloramid dressings. (Case 1.)

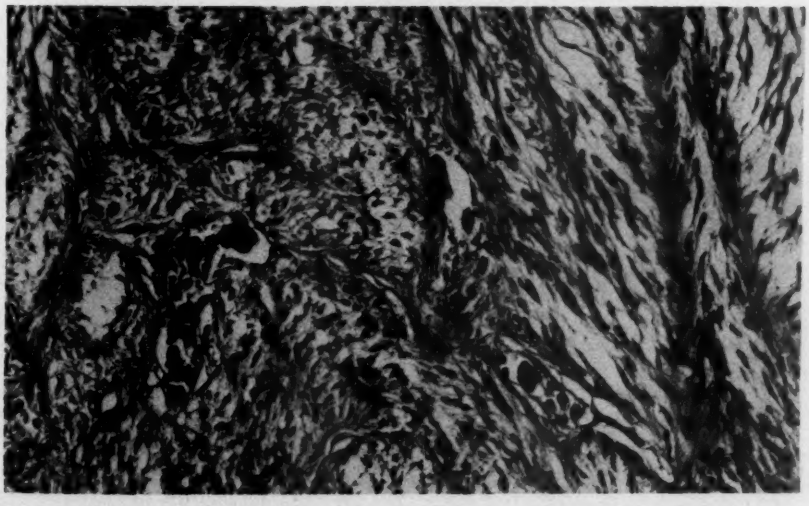

Fig. 2. Histologic structure of the tumor shown in fig. 1.

to thirty minutes. During this process much of the epithelial debris and secretion was washed away. Following this a large pad of gauze—six to eight layers in thickness—saturated in azochloramid in 1:500 triacetin solution was applied directly to the wound and covered with some rubberized silk; over this a layer of bandaging was applied. The bandaging usually remained in place until the following morning. On alternate days, the patient found it comforting to repeat her bath in the evening and apply a fresh dressing of azochloramid.

Fig. 3. Appearance of the patient six months after onset of treatment. (Case 1.)

Under this treatment the odor and weeping of the wound were satisfactorily controlled and deep x-ray therapy was continued without any untoward effects on the surrounding normal skin. The only complaint of the patient in regard to the treatment was a slight stinging or burning sensation which lasted for only a few minutes immediately following the application of the fresh dressing.

In the course of the next three months, following the completion of the deep x-ray therapy and the continued use of daily azochloramid dressing, the surface of the wound entirely healed and the tumor in the upper portion of the thigh shrank until it was nearly level with the surface of the skin.

In March, 1937, a year after treatment had been begun at this clinic, the patient returned for observation because of extension of the lesion down the leg. This time the lesion did not fungate. X-rays of the chest at this time disclosed numerous metastases in the mediastinum and left lung. The patient died April 18, 1937, from pulmonary embolism, having been entirely ambulatory and free from any odor or discharge from the lesion during the last nine months of her illness.

CASE 2.—The patient, a white man, aged 37, was first seen Sept. 24, 1936, with a swelling beneath his right knee. On July 5, 1935, a wart appeared in the region of his right ankle. This was removed in November, 1935, but no microscopic study was made. The tumor came back promptly and was about 3 cm. in diameter. It regressed under eight weeks of x-ray therapy given

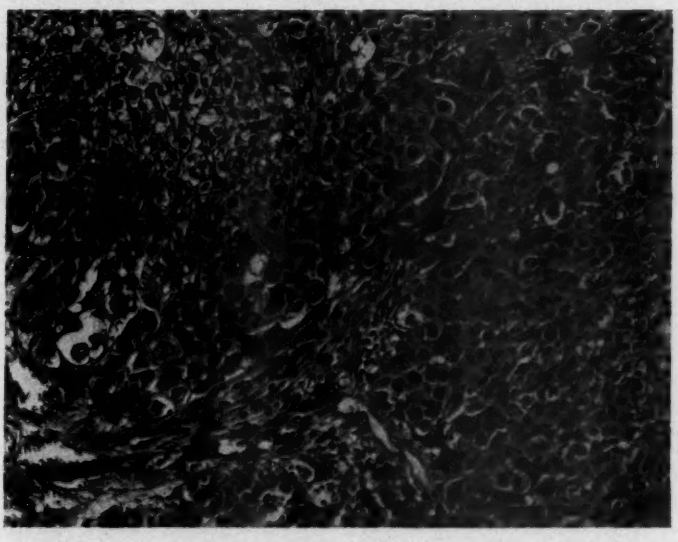

Fig. 4. Photomicrograph of the lesion in Case 2.

prior to March, 1936. In May a swelling appeared behind the right knee in the popliteal space. This was given x-ray treatment but did not improve. At the time of examination at this hospital in September, there was a pigmented scar in the region of the right ankle, a hard mass the size of two fists in the popliteal space and an enlarged inguinal gland in the right groin. The inguinal gland and a portion of the tumor in the popliteal space were removed for biopsy September 29. The microscopic examination showed the tumor to be a grade 4 epidermoid carcinoma. The patient was discharged from the hospital October 6. At this time the incision in the inguinal region had healed, but there was a small amount of drainage.

The patient was re-admitted Dec. 11, 1936, for further treatment. At this time there were two fungating and ulcerating masses in the popliteal space, each about 2.5 cm. in diameter. These bled whenever the dressing was removed and exuded pus and a foul odor. The incision in the right groin had healed but there were several large nodes in this region. The patient had a painful swelling at the right elbow. An x-ray examination revealed a destructive lesion of the lower end of the humerus, apparently metastatic in origin.

The painful mass in the region of the elbow was treated by deep x-ray therapy between January 1 and February 25. Under this therapy the mass decreased in size, pain was minimal and considerable motion returned to the elbow joint although no re-ossification occurred. The fungating lesions in the popliteal space were treated with azochloramid dressings. Gauze saturated

in a 1:500 triacetin solution was applied daily following a tub bath and the dressing was allowed to remain in place 24 hours. Under this mode of therapy the odor of the fungating wound and the amount of pus grew steadily less. The dressings were applied daily from December 12 to February 26. During this period of time palliative deep x-ray therapy was given to the fungating tumor through an 8 by 6 port for a total of 3,200 R. Between February and April the discharge and odor from the wound in the popliteal space continued to be controlled satisfactorily with azochloramid dressings and tub baths. The patient was able to receive visits from his friends without embarrassment which heretofore he had experienced because of the obnoxious odor.

Early in April the neoplastic mass in the popliteal space began to grow rapidly and contractures at the right knee were such that dressings were applied only with difficulty. The patient became bedridden and developed metastases to the left femur, left inguinal gland and numerous subepidermal metastases over both legs and over the right arm. The mass in the lower right humerus grew rapidly. He died May 10, 1937.

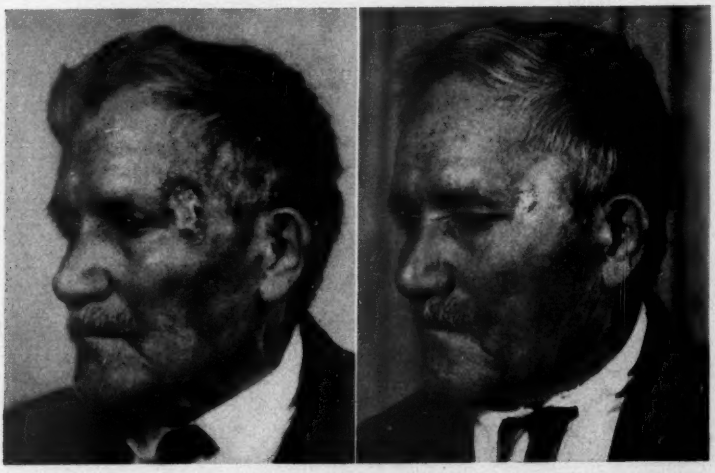

Fig. 5. Squamous cell carcinoma of left temporal region before treatment. (Case 3.)
Fig. 6. The same patient after treatment.

Case 3.—The patient was a white man, aged 76, who had always enjoyed good health. About two years before he had noticed a sore in the temporal region on the left side of his face. There was no pain. He treated it with salves and ointments but the sore did not heal. Two years after the onset of his trouble he presented himself for treatment. Examination revealed a shallow dirty ulcer, lateral to the left eye. The base was sunken, yellowish in color, the border elevated and pearly in appearance. The lesion measured 5 cm. in diameter.

A biopsy was taken and disclosed squamous cell carcinoma, and deep x-ray therapy was begun April 27, 1937. During the first course of deep x-ray therapy, because the secondary infection failed to regress and because of the foul discharge from the wound, azochloramid dressings saturated in 1:500 solution in triacetin were begun.

Azochloramid dressings were applied every other day in the out-patient department. These were continued from May 14 to June 14, during which time the wound improved and showed a clean granulating base and a tendency toward healing. At the end of July, the lesion began to heal rapidly. On examination September 21, the lesion was one-fourth its original size. There was a dry scab over its surface. There was no weeping and no odor.

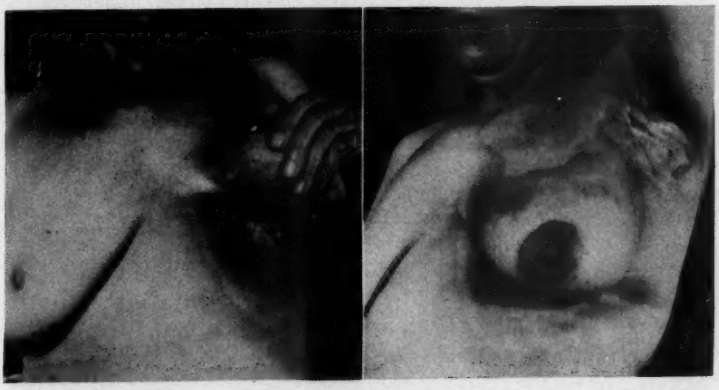

Fig. 7. Ulcerated mammary carcinoma. (Case 4.)
Fig. 8. The axillary involvement in the same case. These photographs were made before treatment was instituted.

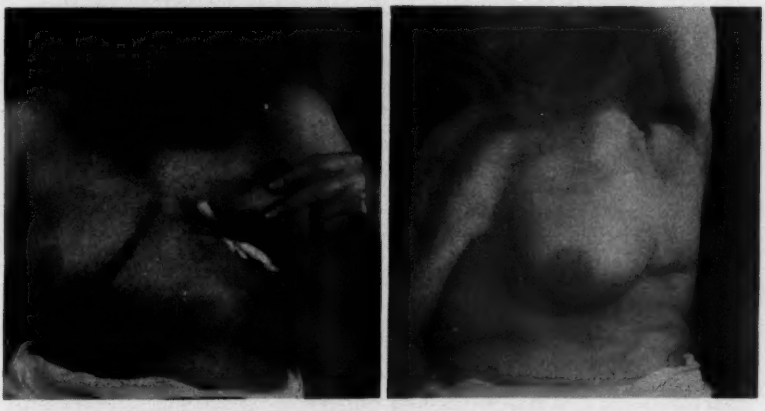

Fig. 9. The appearance of the breast after treatment as described in the text. (Case 4.)
Fig. 10. View of the axilla after treatment.

CASE 4.—The patient was a white woman, aged 64, who noticed a lump in 1934 at the lower margin of the left breast. This grew gradually and became ulcerated about a year after onset. About nine months after this a second mass developed in the left arm pit. On examination the patient was pale and anemic and had lost over 30 pounds in weight. There was a large ulcer on the under surface of the dependent portion of the breast 6 by 4

cm. in diameter with a necrotic base and indurated edges. Surrounding the ulcer there was a large mass which measured 9 cm. in diameter. A second ulcer measuring 3 cm. in diameter of similar character was found in the left axilla. This was surrounded by an indurated mass. The skin over the lower left breast showed lymphedema. A foul odor accompanied the discharge from the wound. X-ray therapy was begun in July, 1937, but despite treatment the base of the ulcer remained necrotic with a foul discharge. On August 2, during the course of x-ray therapy, daily dressings of gauze saturated with azochloramid 1:500 in triacetin solution were applied following a preliminary bathing of the wound with boric acid solution. By the 23rd, the indurated masses about the ulcers had softened under x-ray therapy. The lymphedema of the skin still persisted. The base of the ulcers had a clean appearance and the lesions were without conspicuous odor. At this time dressings were applied every other day. On September 15, the ulcers had a granulating base and were without odor. In November the ulcerated areas had healed.

The bactericidal and deodorant action of azochloramid is dependent on its mild and selective oxidizing properties. In the presence of a mixture of organic materials it will oxidize only those of intense reducing power. Guiteras and Schmelkes[1] investigated the oxidizing action of this antiseptic in the presence of various organic substances. They found that azochloramid, after contact with glycine for 24 hours, had lost only 5 per cent of its chlorine content, whereas after contact with cystine it had lost 20 per cent of its chlorine content. Similarly, after contact with gelatin (sulphur-free protein) only 1 per cent of its chlorine content had been lost, whereas after contact with egg albumin (sulphur-containing protein) it had lost 5.2 per cent of its chlorine content.

Exudates on the surface of a fungating tumor contain reduced sulphur compounds, as indicated by the odor. Application of azochloramid to such a lesion selectively oxidizes and deodorizes these sulphur compounds. Other chlorine compounds, such as chloramine-T and Dakin's solution, do not show this selective action and while they, of course, also oxidize the ill-smelling sulphur compounds, they in addition oxidize all other miscellaneous organic matter and in doing so are used up rapidly, so that it is necessary to replace them at frequent intervals. Azochloramid dressings on the other hand retain the deodorizing effect for 24 hours or longer.

In addition, azochloramid is strongly antiseptic retaining its ability to kill micro-organisms in the presence of organic matter. In being able to do this, it disinfects such lesions which, due to the large amount of necrotic material, are otherwise fertile media for bacterial growth. Once such a lesion is sterile the application of the antiseptic prevents invasion by pathogenic organisms.

1. Guiteras, A., and Schmelkes, F.: The Comparative Action of Sodium Hypochlorite and Chloramine-T, and Azochloramid on Organic Substrates; Vol. 104, p. 235, 1934.

REGIONAL ILEITIS

(With Republication of a Case Reported in 1806)

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REGIONAL ileitis is an acute, subacute, or chronic necrotizing and cicatrizing inflammatory condition of the terminal ileum. This designation and definition was given in 1932 by Crohn, Ginzburg and Oppenheimer[1] following the study of 14 cases, in 13 of which pathologic specimens were obtained at operation. In their opinion the clinical picture, the gross and microscopic appearance of the involved tissue constitute a syndrome unlike anything previously reported. The rather complete review of the literature of granulomas of the small intestine in 1920 by Tietze convinced them that a new entity was being described. The reports of Moschcowitz and Wilensky[2] in 1923 concerning 4 cases of benign granuloma of the intestine, contained one detailed case involving the terminal ileum which had some of the features of ileitis. Crohn and his associates however did not believe this isolated case paralleled the disease they had observed. Mock's[3] description in 1931 of granuloma of the intestine dealt chiefly with lesions in the cecum, thought to have arisen from the site of an appendiceal stump and likewise did not compromise the priority of their entity. In reviewing the earlier literature however we encountered an interesting communication with sufficient similarity of detail to question this priority of description. The report, which will follow in full, was presented by Drs Charles Combe and William Saunders[4] before the Royal College of Physicians in London, July 4, 1806.

A SINGULAR CASE OF STRICTURE AND THICKENING OF THE ILEUM.

William Payne Georges, Esq., of a very nervous and delicate habit, had been for many years troubled with flatulency and complaints in the bowels, attended with costiveness and a quick pulse, which generally beat between 90 and 100 in a minute. Toward the end of September, 1805, he had an irregular intermittent fever. From this time all his former complaints rapidly increased. He especially complained of wind and great costiveness, and about 2½ or 3 hours after eating, of excessive pain in the bowels. So intense was this pain that for the last three weeks he refused taking any solid food, and subsisted entirely on jelly, broth, milk, etc., and these only in a very small quantity, always dreading the pain that succeeded even this kind of food. When he had a natural stool, it was passed in very small indurated lumps, either separate or attached together, having some resemblance to sheep's dung. His inconvenience continued to increase to the time of his death, which took place early on Sunday morning, February 9th, 1806, at which time he was more emaciated than any person we had ever witnessed.

On the next day the body was opened by Dr. Combe in the presence of Dr. Saunders and the following appearances were observed. There was not any fat between the skin and the muscles of the abdomen, or about any of the parts of the integuments. The epiploon was entirely wasted and there was not the least appearance of fat about the mesentery or kidneys. The liver, pancreas, spleen and kidneys were in a sound state. The stomach, though rather smaller than normal, was in a normal state, as was the duodenum, the jejunum, and the upper part of the ileum. The lower part of the ileum as far as the colon, was contracted, for the space of three feet, to the size of a turkey's quill. The colon had 3 constrictions, one about 3 inches long at the distance of 7 inches from the caecum, a second about 1 inch long at the distance of 4 inches from the former and a third not quite half an inch long at the distance of 3 inches from the last.

Wherever the intestines were constricted, the coats were very much thickened and exhibited an appearance of inflammation; while the blood vessels, passing through the mesentery of the intestines, were enlarged.

The time at which Mr. Georges perceived the great pain and uneasiness to commence after eating, corresponds with the period at which the food would naturally arrive at the beginning of the constriction of the ileum. The figure of the stools we apprehend arose from the constrictions of the colon.

This history of a singular case of stricture and thickening of the ileum presented in 1806 is interesting in that it so closely resembles the characterization of the more recently described ileitis. The complaint of many years duration, the extreme emaciation, the bowel cramps, and the marked constriction and thickening of the terminal ileum with the appearance of inflammation is typical of the chronic, cicatrizing stage of regional ileitis with the clinical symptom of bowel obstruction. The findings in the colon are corroborative evidence. There the small segmental involvement of the same character as the lesion in the ileum coincides with Colp's description of a combined form of ileitis and colitis.

The disease when described in 1932[1] was thought to occur in the ileum alone as an acute, subacute or chronic inflammatory process affecting mainly young adults. In the discussions that ensued it was suggested that a similar involvement of other portions of the small intestine might in time be encountered. This prophecy was made good in 1933 when Harris, Bell and Brunn[18] found the identical process in the jejunum. The following year Colp reported the first case of combined ileitis and colitis with operative and pathologic studies. Crohn and Rosenak[5] substantiated this in 1936, presenting 60 cases of terminal ileitis with 9 of simultaneous involvement of the colon. From this observation and studies of the specimens they believed the concurrent invasion of the small and the large bowel to be by a similar, nonspecific inflammatory process with the ileum reacting to the influence as a granuloma, and the large intestine responding as an ulcerative and hyperplastic colitis.

The disease usually appears between the twentieth and thirtieth years and twice as often in males. This is not a widespread disease since Jackson[6] found only 219 cases reported in the American literature from the time of Crohn's description in 1932.

The essential cause remains unknown in spite of much clinical investigation. Reichert and Mathes[7] injected sclerosing substances in the lymphatics of the mesentery and subserosa of 19 dogs. In several animals a suspension of *bacillus coli* was given intravenously before the lymphatics were injected. Those specimens showed the most marked changes. Histologically the bowel wall in all was greatly thickened and edematous and infiltrated with leukocytes but with no ulceration of the mucosa. Even after a single injection chronic changes existed for months. They found no evidence of blood vascular thrombosis and Bell[8] was unable by interfering with the intestinal blood supply to produce an ulcerative cicatrizing enteritis. Reichert and Mathes concluded that the disease in man was likely due to a chronic low grade bacterial infection.

The disease frequently runs a fairly constant and typical clinical course being either acute and fulminating from the onset or chronic of several months duration when first observed. The rapid phase may simulate any acute intra-abdominal inflammatory condition, especially appendicitis. The common features of abdominal cramps distributed to the lower right quadrant, tenderness, rigidity, fever and leukocytosis may make the two diseases indistinguishable. The picture may recur or give way to a chain of symptoms suggesting ulcerative colitis, with diarrhea the outstanding feature. Characteristically, however, chronic ulcerative colitis is manifested by a greater frequency of bowel movements, with attendant generalized abdominal cramps and greater quantities of blood, mucus and pus in the stool. Anemia, weight loss, malaise and slight fever may be noted in either disease after several months. Chronicity leads to fibrosis, thickening, stenosis, obliteration, deformity and obstruction. This seems to be the evolution of ileitis when it fails to resolve spontaneously. The presenting symptoms obviously will be obstruction with diffuse abdominal cramps, nausea, vomiting, distension and borborygmus. Loops of bowel may be apparent or a mass may be felt in the lower right quadrant. There is a marked tendency for the bowel to become adherent to the anterior abdominal wall and adjacent viscera, more frequently the right colon, but also the sigmoid. A mass results which can easily be felt through the abdominal wall or by rectum. It was present in a high percentage of Crohn's[1] cases and he emphasized this finding as being rather characteristic of ileitis. The inflammation frequently does not subside at this period but perforates, rarely into the free abdominal cavity, but

through the abdominal wall, into the mesentery, the colon or the small intestine with fistula formation. It is believed that a number of persistent and intractable fistulas following the drainage of supposed appendiceal abscess are due in reality to ileitis. The finding at subsequent operation for fistulectomy of an apparently normal appendix seemed to suggest this course.

The diagnosis in the acute phase may be particularly difficult because of its mimicry of acute appendicitis. The experience of Koster and Kasman[9], and of Crohn[1], bear out this statement. Fourteen of 31 of their patients had undergone appendectomy for their complaint. With progression, recurrence and chronicity, symptoms are added which are likely to aid in differential diagnosis. Chief among them is the appearance of an abdominal tumor, more frequently in the lower right quadrant. It results from the plastic process which tends to make the small intestine confluent with the colon or other viscera. Crohn[1] lays great stress on this finding which with the usual manifestations is more typical of ileitis than primary tumors of the right colon or small intestine, or appendiceal abscess. When diarrhea and the symptoms of enteritis are most marked the condition must first be differentiated from chronic ulcerative colitis. The frequency and urgency of bowel movements, the presence of blood, pus and mucus in the stools, the apparent anemia and cachexia are not in themselves incontrovertible diagnostic evidence of either ileitis or chronic ulcerative colitis. Likewise, fistulas are common to both. However, in ileitis fistulas more frequently occur in the lower right abdomen while with chronic ulcerative colitis they are found as fistulae in ano. As every one knows chronic ulcerative colitis begins in the rectum in 90 per cent of cases and tends to spread proximally to involve the colon. However in fulminating and long standing cases retrograde extension to the ileum may take place. With rectal involvement the proctoscopic picture is diagnostic. X-ray studies are valuable to show segmental disposition or the extent of colonic involvement but are of little aid in portraying the rectal lesions.

Kantor[10] has made a useful roentgenologic observation in ileitis which is probably the greatest single aid in making the diagnosis. Investigation of the small intestine had been previously neglected. The normal patterns were not established and consequently interpretations of lesions of the small intestine were more difficult than in any other portion of the gastrointestinal tract. He utilized the standard opaque meal and made hourly observations beginning approximately five to six hours after the ingestion or just before the cecum began to fill. The most striking finding was the "string sign." It was characterized by a thin, slightly irregular, linear shadow sug-

gesting a cotton string in appearance which extended from the area of the defect in the ileum to end at the ileocecal valve. When present, he believed this sign indisputable evidence of ileitis but mentioned several sources of error to be avoided. A well filled appendix dipping into the pelvis is most likely to confuse if one does not remember that it gives a more homogeneous shadow. The sacroiliac joint shadow falls in the line of the field examined but can be identified as such by comparing with the opposite side. Spastic segments of small bowel display a wider lumen, a denser shadow, a smoother outline and a varying position. The "string sign" of ileitis, on the other hand remains constant for hours or even days. Tuberculosis, syphilis and stenosing sarcoma of the terminal ileum may occur, but roentgen studies of these rare lesions have been few.

The roentgenologic description of regional ileitis was written before it was known that a similar pathologic process could coincidentally affect the colon. It was already known that chronic ulcerative colitis could extend into the ileum. Obviously then it became necessary to distinguish cases of ileitis with involvement of the colon from chronic ulcerative colitis and involvement of the ileum. Weber and Bargen[11] have given a clear cut picture of chronic ulcerative colitis as it invades the colon. In the earliest stages, hyper-irritability manifested by extreme spasm may be the only sign, but it is unusual not to find some of the typical signs, namely, narrowing, shortening, loss of haustra and destruction of the mucosa. The colon fills rapidly, the lumen is reduced, redundancy disappears, the bowel straightens and becomes hard, stiff and inflexible. Deep destruction of the mucous membrane gives a feathery and moth-eaten appearance. Isolated segments in the proximal colon are rare. The long segments will display the characteristic features of chronic ulcerative colitis, but the shorter ones may strikingly resemble cancer. It is distinguished however by its regular canalization and tendency to concentric deformity. The diagnosis of ileitis, primary or secondary to chronic ulcerative colitis will depend more on the roentgenologic findings than all other clinical aides. Confusing the acute cases with appendicitis, however, will continue. Special investigation is not likely to develop as a routine in patients with acute abdominal complaints.

Pathologically the early specimen of bowel is soggy and edematous with hypertrophy of the lymph glands and thickening of the mesentery. The serosal surface is smooth without exudate but markedly congested and mottled as in a vascular accident but there is no evidence of intussusception, constriction or thrombosis of the mesentery. It looks friable as if it would rupture with the slightest

handling, and it will rupture in the acute, fulminating stages. In the chronic and fibrostenotic stages the serosa loses its gloss and frequently exhibits tubercle-like structures on its surface. The involved segment is narrowed and thickened, and well demarcated from the proximal part of the bowel which is dilated. With the marked tendency to perforation there may be encountered fistulas between loops of small intestine, the right colon or sigmoid, any adjacent viscera, and the anterior abdominal wall. Abscesses are encountered but rarely does free perforation into the abdominal cavity take place.

The process in the ileum due to an extension of chronic ulcerative colitis is different. It is denuding, similar to the reaction of the same process in the colon and not hyperplastic and granulomatous as in primary ileitis. Crohn and Rosenak[5] have reported 9 cases of a combined form of primary ileitis and colitis with distinct and characteristic x-ray, clinical and pathologic findings. In their series one case was thought to represent the simultaneous onset of primary ileitis and primary chronic ulcerative colitis. Recurrence took place following resection of the ileum and colon. Another one of the cases was considered primary ileitis with secondary, but not simultaneous colitis. Berg[12] holds that primary ileitis is only another manifestation of chronic ulcerative colitis. There remains much confusion as to the nature of the combined involvement of the ileum and colon.

The treatment of ileitis is immediately divided into the medical and surgical management. Sufficient time has not elapsed for evaluation of the benefits of each as regards cure, prognosis to life, incidence of recurrence and end results. There have been cases treated medically from the start with cures. There have been others subjected to exploration which revealed such extensive involvement of the intestine that resection seemed imminently dangerous and the operation was terminated without interference. Some of these cases have responded to medical care. Such ones are likely to be the very acute, of one to two weeks' duration with a thickened, soggy, edematous terminal ileum with blotchy, red serosa, thickened mesentery, and hyperplastic glands. Because spontaneous resolution has taken place in such cases, and because of the incidence of recurrence in some of the operative cases, medical management for all has been advocated by some. It must be allowed that there is no one fixed method of treatment and that the nature of the individual case will often decide the procedure. There is a greater number of reported cases where some form of surgery has been instituted. In the main there are three procedures available, ileocolostomy alone, ileocolostomy followed in a few weeks by resection of the diseased ileum, cecum, and as much of the right colon as may be involved; or, the radical operation can be completed in one stage, consisting

of ileocolostomy and resection. Lewisohn[13] has reported five ileocolostomies for extensive and severe ileitis, with good results as indicated by a gain in weight, reduction in diarrhea and general improvement. Meyer[15] believes that with limited inflammation ileocolostomy is sufficient. On the other hand Mixter[16] prefers one stage resection unless abscess or fistula exist. Most will agree that the risk of ileocolostomy is less than with radical resection, but the end results are more satisfactory with the latter. Probably Dixon[17] more closely approaches the solution when he advocates ileocolostomy for the poor risks, and lets the subsequent course determine the second operation. However, he has found that approximately 50 per cent of these will require resection. When the patient's general condition is satisfactory and the process is a localized or regional ileitis, as has been frequently assumed, the best results should come from complete removal of the diseased area. The few instances of recurrence where radical resection has been done is not sufficient reason to decry the procedure. It is probable that in such cases slight or subclinical involvement persisted, which was not appreciated at the time of operation, and served as a focus for the reactivation.

Our attention has been only recently revived in regard to this entity and more time and specific knowledge will be required before determining the prognosis, best method of treatment, incidence of recurrence, morbidity and mortality. In the recent literature Crohn has reported the mortality of 17 cases unoperated on, as 3 deaths, or 17.6 per cent; and of 51 cases operated upon as 5 deaths or 9.8 per cent. The 17 cases were diagnosed clinically, by x-ray and in 5 by exploration. Three of the total died from peritonitis and exhaustion, one had to undergo resection after two years of a downhill course, four were doing seemingly well, four were not improving, and the remaining cases were lost to follow-up study. Koster and Kasman[9] reviewed the literature and were able to state that the general mortality was 14 per cent. Of the 65 cases in which resection was performed there was a recurrence of the original lesion in spite of radical resection in 10 or 15 per cent. Simple side tracking operations in 15 cases resulted in a cure in 13, death in 1, and persistent external fistula in the remaining one. Eight early cases were cured without intestinal surgery.

The following three cases represent rather typically the findings in the acute phase. The management and other features will be discussed.

Report of Cases

Case 1. On Nov. 24, 1936, a white girl, 18 years old, was brought to the hospital. She had always been "weakly." For five or six years she had suffered

abdominal pain, cramping in character and general in extent. This had often been associated with nausea and vomiting but never with diarrhea or blood and mucus in stools. She had experienced no indigestion or dyspepsia.

The present attack had begun two weeks earlier with persistent pain in the right lower quadrant of the abdomen. She had had no nausea, diarrhea or constipation. The pain did not radiate. Her temperature had been from 99 to 100 on the several occasions when her doctor took it.

She was thin and pale. Examination showed a hard, slightly tender mass in the lower right abdomen, but nothing else of importance. Digital examination of the rectum was negative. The urine was normal. The white cell count was 7200 with 65 per cent polymorphonuclears.

Two days later she was operated on with a diagnosis of appendiceal abscess. The mass in the right lower quadrant was found to be the greatly enlarged, edematous mesentery of the ileum, cecum and first half of the ascending colon. The terminal six inches of the ileum, the cecum and part of the ascending colon were shiny red and felt rubbery. There was no free fluid and no evidence of obstruction. An attempt was made to mobilize the ileum and cecum for resection, but bleeding was great when the cecum was freed from the lateral abdominal wall, to which it was firmly adherent. The condition was thought to be tuberculous and a side-to-side ileocolostomy was done, uniting ileum to transverse colon. We intended to resect the terminal ileum and proximal colon at a later date, but the patient made a quick recovery. She left the hospital in three weeks and was not seen again until requested by letter to return for examination a year later. At that time she had gained 30 pounds and she said that she had been quite well.

Physical examination and routine laboratory studies were essentially negative. Barium enema showed that the colon filled normally. The enterocolostomy was patent and the ileum distal to the stoma filled without narrowing, fixation or defect.

The excellent recovery in this case may have been due to the four weeks rest in bed following the operation but we are inclined to think the ileocolostomy should be given the major credit.

CASE 2. A white man, 32 years old, was admitted to the hospital March 6, 1937, complaining of pain in the abdomen. The pain had begun one week prior to admission as a generalized dull ache. In two or three days it became localized to the right lower quadrant. He had had no nausea or vomiting, no diarrhea and no blood or mucus in his stool. No previous history of indigestion or abdominal pain was obtained except one attack six months ago similar to this one, which lasted three days.

He looked healthy. Temperature was 100, pulse 110. His weight was 190 pounds. A moderately tender mass in the right lower abdomen with some involuntary muscle spasm was noted. There was no distention nor evidence of fluid. Rectal (digital) was negative.

A diagnosis of appendiceal abscess was made and he was operated on shortly after admission to the hospital. The operative note:

"There was a mass at the ileocecal junction which proved to be greatly edematous and enlarged mesentery. The ileum was shiny red, greatly thick-

ened for a distance of 4 inches proximal to the cecum. The cecum was not inflamed. The mesentery of the ileum was thick and edematous for 12 inches proximal to the cecum, limiting the mobility of the ileum. There was no obstruction. There was no pus in this mass. There was a small amount of clear fluid in the abdomen but no evidence of tuberculous peritonitis. The appendix was grossly normal."

A side-to-side ileocolostomy was done and the appendix was removed to prove its part, if any, in the origin of the process. It was reported as chronic catarrhal appendicitis. He had a disagreeable convalescence, complicated by pain and redness along the left saphenous vein below the knee. He left the hospital 21 days after the operation. Weight 175 pounds.

April 29, 1937. He felt much better. He still had some abdominal pain, but no diarrhea or constipation. Weight 184 pounds.

June 6, 1937. He felt as well as ever. Weight 193 pounds. Appetite and digestion were good. Bowels were moving normally without cathartics. X-ray: Barium filled the colon normally. Just to the right of the midline the transverse portion showed an anastomosis with the ileum. The small bowel distal to the stoma filled well. There was a little irregularity in the lumen close to the ileocecal valve, probably due to inflammatory changes.

We have not seen him since this date but believe that he is well as he promised to return if he had further trouble.

CASE 3. A colored man, 23 years old, was admitted to the hospital on May 7, 1937. For two weeks he had had vague pain around the umbilicus. This had been cramping in character but not accompanied by nausea, vomiting or diarrhea. Fifteen hours before admission he had been seized suddenly with severe pain in the lower right abdomen. This radiated to the right lumbar region and into the right groin. It had been so severe it "doubled him up." He had had difficulty in voiding because of intense pain over bladder when he did so. He had not vomited but had been nauseated. He had had occasional cramping pain in lower abdomen for six months. There had been no loss of weight and he had continued working until two weeks ago. He had never had diarrhea, constipation or blood in stools.

He was acutely ill. Temperature was 100.4, pulse 88. The abdomen was rigid throughout with marked tenderness in the lower half. Slight distention was noted, but there was no tenderness in flanks, nor signs of free fluid. No mass was felt. The rectum was normal on digital examination. White cell count was 16,500, polymorphonuclears 81 per cent. Urine showed a trace of acetone.

Operation was done two hours after admission. Diagnosis, acute appendicitis with perforation and diffuse peritonitis. On opening the abdomen the terminal 8 inches of the ileum was red, shiny, edematous and fixed. The corresponding mesentery was enlarged and edematous. There was turbid fluid and exudate throughout the abdomen and plastic exudate in patches on the terminal ileum. There was probably a small perforation near the mesenteric attachment somewhere in the diseased ileum, though this could not be found. There was no odor. We thought he was too ill for ileocolostomy and resection was out of the question. We removed his appendix for study. The pathologist reported this to be normal except for acute inflammation in the serosa. Three cigarette drains were placed in the lower right abdomen. He made a slow, painful recovery, marked by loss of weight, abdominal cramping and disten-

tion, and temperature from 99 to 102. He left the hospital June 6, 1937. At that time he was draining a small amount of pus, the wound was almost healed and his daily temperature was 99.5 maximum.

June 1. Chest X-ray negative. We asked him to return for further surgery in two months.

July 24. He was readmitted to the hospital on account of headache, pain in neck and vomiting for two days. He had been gaining strength and weight and had had no abdominal symptoms. For 24 hours he had been drowsy. The spinal fluid was cloudy, containing 13,000 cells, predominantly polymorphonuclears. The infecting organism was not identified. He died of meningitis six days later, without exhibiting any abdominal signs. Autopsy was refused.

Discussion

In two of our three cases a mass was felt in the lower right part of the abdomen. In the third a diffuse peritonitis resulted in rigidity of the abdominal wall and the mass, though present, was not felt preoperatively. In none of the three was there any diarrhea, blood or mucus in the stools to suggest ulceration of the mucosa as the primary lesion. In the two who recovered there was no filling defect or spasm to indicate residual ulceration or inflammation, except one small questionable area in the ileum of Case 2 three months after the acute illness. Whatever the ideal surgical procedure may be, we are quite certain no experienced surgeon would have undertaken radical surgery in any of our three patients.

The disease when its symptoms are acute will continue to be treated surgically under the mistaken idea that it is appendicitis. When the condition is recognized at operation it is quite possible we may close the abdomen without further surgery or restrict ourselves to the less radical procedures since they have proved effective in our small series.

Our ideas about the proper treatment of acute salpingitis have been revised greatly during the past twenty years and it seems not unlikely that we may change our views in regard to ileitis also. Time may prove that surgery is not indicated except when perforation, obstruction or persistent sinus is present.

In our third case tuberculosis of the small bowel and mesentery, followed by tuberculous meningitis cannot be excluded. It seems unlikely, however, when we consider the sudden onset, the absence of diarrhea at any time, the bright red ileum, the enlarged fixed mesentery, and the spinal fluid findings.

Summary

1. Ileitis represents an acute, subacute, or chronic necrotizing and cicatrizing inflammatory condition occurring in young adults. Males are affected about twice as often as females.

2. The cause is unknown: no specific etiologic factor has been established but the most probable influence seems to be a low grade infection.

3. The clinical behavior in the acute stages simulates several conditions giving rise to an acute inflammatory condition, particularly appendicitis. The chronic stage with stenosis almost invariably is manifested by obstructive phenomena, a mass in the lower right abdomen, or fistulas.

4. Pathologically the ileum is soggy, edematous and mottled with a thickened mesentery and hypertrophied glands. The chronic stage shows stenosis and fibrosis.

5. X-ray findings of the barium-filled bowel is the most valuable diagnostic aid.

6. Medical treatment is of value in selected and very ill cases, but surgery seems to offer the highest percentage of permanently satisfactory results in the cases reported to date.

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ULCERATING EPITHELIOMA OF THE CHEEK

Case Treated with 500,000 Volt Therapy

HARRY F. MERSHON, M. D.

Los Angeles, Cal.

History: The patient was a white male, aged 52. At the age of 18 he was injured on the right cheek by a baseball. Later a spot appeared in this region which continued to scab and gradually increased in size. Three years ago this had increased to the size of his fingernail. The only treatment had been blood tonics and ointments applied locally. His general health was and had been good.

Examination: On Oct. 29, 1936, examination revealed an irregularly shaped, deeply ulcerating tumor on the right cheek, involving the right outer canthus, approximately 4 cm. in diameter. The eyelids were closed and it was felt that the conjunctiva was also involved. The biopsy showed a squamous cell epithelioma, Grade 1 (fig. 1).

Fig. 1. Photograph of patient, Oct. 29, 1936. Fig. 2. After x-ray treatment, Mar. 4, 1937.

Treatments: The patient was given a series of x-ray treatments to a 10 by 10 cm. area over the involved site, with the half million volt supervoltage x-ray machine. The factors were 500 KV., 4MA., 0.8 mm. lead filter, 50 cm. distance, 15 R per minute intensity, and a wave length of .05 angstrom. One hundred fifty R units were given daily, extending over a period of 25 calendar days, to a total of 3,000 R units.

Erythema began to appear on the eleventh day and gradually increased. On December 4 the reaction was beginning to fade, the edges of the lesion were softer and the area was smaller. The patient was seen at intervals of from four to five days until March 4, 1937, at which time the reaction had subsided; there was no evidence of disease, and the outer canthus was beginning to fill in. (fig. 2).

On May 24 a beginning recurrence in the lower lid received a small amount of further treatment. On Nov. 8, 1937, there was no evidence of disease and a plastic surgeon plans to complete the fill-in of the outer canthus.

From the Oncological Service of Drs. Soiland, Costolow and Meland.

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CORONARY DISEASE AND THE SURGEON

HEART disease is today captain of the men of death. Heart disease ranks first as a cause of death in the United States, and it accounts for more deaths than the next three most common causes combined. From *The Journal of the American Medical Association* of April 16, one learns that 3,277 American physicians died during 1937:

> Heart disease was reported as the cause of death in 1,360 cases...Arteriosclerosis was listed as the third most frequent cause, with 382 deaths. Fourth on the list was cerebral hemorrhage, with 353 deaths; 20 additional cases were reported as due to paralysis...The number of cases in which hypertension was reported was 91.

That is to say, more than two thirds of the doctors who died in this country last year succumbed to cardiovascular disease!

The coronary arteries, it is true, were mentioned in only 387 of these deaths. It is however likely that cardiac infarction was responsible for many more: of nine doctors who died in the city of Atlanta, seven died of heart disease, five unquestionably with coronary thrombosis, the other two probably with the same trouble. As Stewart Roberts has said, "The coronary artery may well be called the doctor's artery."

It is appalling economic waste, to say the least, to have so many doctors, skilled through expenditure of money and effort over years, struck down in their prime. Each one of us, moreover, has a deep, intensely personal interest in the heart, for each one of us nurses a certain apprehension, even though he confess it not to himself, as to the condition of his own coronary arteries. And rightly so.

Adequately to fight a disease one should remove the cause. What is the cause of sclerosis of the coronary arteries? What indeed is the cause of arteriosclerosis anywhere? We might as well admit that we don't know very much about the cause of sclerosis of any artery, but let us review the little we do know.

On examining large groups of vital statistics we find that coronary sclerosis occurs much oftener in persons who are overweight, and it is particularly common in diabetics. Diabetes, as has long been known, is also much more common in the obese.

We know too that arteriosclerosis tends to run in families: a century ago Hawthorne, though not a physician, described such a family in *The House of Seven Gables.*

Coronary disease is an all too frequent cause of death among doctors, particularly among ambitious, hard-working ones who devote themselves untiringly and selflessly to the care of their patients. If we try to explain this, the obvious reason is the constant, heavy strain under which he lives. This strain, except when he is away from home, is unremittent, for the doctor is on call twenty-four hours a day. The strain is severe too, for the doctor carries the responsibility for the lives of individuals who know him and trust him. The responsibility for human life, even for that of one of the least of these, is greater than any other and this responsibility is acutely intensified for the surgeon.

Not the least of the doctor's worries, especially in these parlous times, is to provide for those dependent on him and to leave them a competency in the event of his untimely death. A good name may be a source of pride and joy to his widow and children, but it won't feed them, clothe them, nor house them. And a superlative name won't buy the poor orphans geographies or algebras.

Some authorities have held that tobacco is a factor contributing to coronary disease, but they have not been able to bring forth much evidence in support of their opinion. Some have blamed alcohol, but they have not been able to adduce a scintilla of evidence that is is worth a tinker's dam to uphold their theory. As a matter of fact, Raymond Pearl has recently stated, on the basis of tremendous fig-

ures, that, whereas the person who smokes excessively has a slightly decreased life expectancy, he who drinks moderately has a slight edge on his abstaining brother.

Strenuous or prolonged physical exercise has many times killed a man who for years had made no physical effort more arduous than stepping on the accelerator.

All right then, here is some gratuitous advice for the surgeon who has passed 40 and who does not wish to die of heart disease:

1. Avoid fat more scrupulously than the devil avoids holy water. Find out the average weight for a man of your height and age and make sure that your weight is ten or fifteen pounds below that. If necessary to lose a great deal, go slow.

2. Do not work too hard. Do not take your patients' troubles too gravely to heart. Teach yourself to relax whenever you can. Read, mark, learn and inwardly digest Osler's immortal *Aequanimitas*. Cultivate a hobby. Sleep. Sleep all you can: sleep late in the morning now and then, even though you may keep some patient waiting. If you can't sleep, rest in bed anyway. Take vacations. Take vacations regularly: take them before you have to. Three or four days away from home every few months may be more convenient, as well as more beneficial, than a longer time once a year. Even an athletic trainer knows the danger of his charges going stale. Trust your brother surgeons: learn to turn over your patients to one or more of them when it is advisable for you to be away. Believe that you can do more good for your fellow man and that you can accomplish more work in twenty years of active health than in ten years of constant grind.

Don't run upstairs ever.

Don't drive through downtown traffic as though you were hurrying to do an emergency tracheotomy. It is safer to drive 70 miles an hour on a Florida highway at noon than to drive 30 miles an hour on Peachtree Street at 5 p. m.; and the tax on the coronaries is much less. It is rare that two minutes or ten minutes will make any real difference to your patient.

And, if you have dependents, carry as much insurance on yourself as you reasonably can.

3. If you have taken no exercise since you received your sheepskin, after finding out that your general physical will warrant your doing so now, take up sports again. But work into them gradually. Don't suddenly undertake to prove to your adolescent son what an athlete his old man was and still is: be your age.

Golf is admirable. Nothing is better adapted for taking the harassed surgeon's mind off the woes of the world in general and of his patients in particular, than to chase the white pellet over the greensward. But don't try 36 holes at one fell swoop if you haven't had a club in your hands for ten years. It is much better to shoot 18 holes twice a week the year round (and we can do this in the South) than to try to shoot 36 holes every day for three days running. Don't fret over an 88,—or over a 108; remember that comradeship, sunshine and fresh air are more important than the score. Let the professionals break par.

4. It is not necessary for your hand to be in contact with a rubber glove or a cigarette all of your waking hours. Do not smoke continuously. If you know that you will not have occasion to operate for more than twenty-four hours, do not hesitate (if you like it) to lift a few.

5. Have a yearly physical check by a competent medical man, and have an electrocardiogram as often as he thinks necessary. Pay attention to whatever instructions he thinks advisable in your individual case.

To sum up, while the Golden Rule of Holy Writ is for the good of your soul, for the good of your own heart live always by the golden rule of ancient Greece,

MODERATION IN ALL THINGS.

L. M. B.

BOOK REVIEWS

The Editors of THE SOUTHERN SURGEON *will at all times welcome new books in the field of surgery and will acknowledge their receipt in these pages. The Editors do not, however, agree to review all books that have been submitted without solicitation.*

HEMORRHOIDS. By MARION C. PRUITT, M. D., L. R. C. P., S. (Ed.), F. R. C. S., President, American Proctologic Society; Associate in Surgery, Emory University School of Medicine; Proctologist, Grady Hospital, Crawford W. Long Memorial Hospital, Georgia Baptist Hospital, and Atlanta Antituberculosis Association; Formerly Resident Surgeon, Westminster Hospital, London, England; Lieutenant, Temporary and Honorary Commission, R. A. M. C., Major, U. S. M. C. 170 pages, with 73 illustrations, including 7 in color. Price, $3.50. St. Louis: The C. V. Mosby Company, 1938.

Readers of THE SOUTHERN SURGEON are familiar with the slogan of one of our loyal advertisers, "to do one thing well." That same slogan might have served as the theme of this monograph on hemorrhoids. Dr. Pruitt opens with a discussion of the preclinical aspects of the subject. He then discusses in detail methods of examination, instruments to be used and the desirable types of anesthesia. He classifies hemorrhoids and describes the signs and symptoms on diagnosis. The chapter on differential diagnosis is unusually full. The author is partial to the injection treatment of hemorrhoids but he describes the operative treatment in great detail.

The concluding chapter on the choice and evaluation of methods is a superb summary.

Dr. Pruitt leaves roseate, ornate writing to others: his style is simple but clear as day. The illustrations are excellent. In addition to a number of good original photographs and a few plates that have been published elsewhere, there are a large number of original drawings. Some of these have been drawn from life while some are essentially diagrammatic. Even the several anatomic illustrations which have been borrowed from standard texts of anatomy have been redrawn for the sake of uniformity and emphasis. The Mosby Company has put out its best to make a technical masterpiece of this monograph on piles. It is recommended without reservation to all who aspire to relieve their fellow men of this common ailment.

THE PRACTICE OF UROLOGY. By LEON HERMAN, A. M., M. D., Professor of Urology, University of Pennsylvania, Graduate School of Medicine; Urologist to The Pennsylvania Hospital and to the Bryn Mawr Hospital; Consulting Urologist to the Methodist Episcopal and Burlington County (New Jersey) Hospitals. 923 pages, with 504 illustrations. Price, $10. Philadelphia and London: W. B. Saunders Company, 1938.

Dr. Herman has set out to help the general practitioner and surgeon, but one wonders if his book would not also be good for many specialists in urology. There is a freshness about a first edition that carries its own charm: and the opinion is hazarded that, unlike many firsts, alterations in future editions of this book will be made necessary only by advances in knowledge. Space is wisely apportioned, little being devoted to extremely rare conditions and a great deal to, for example, gonorrhea.

The author of a book must always be confronted with the problem of novelties. If he omits the latest kinks, the book may appear old-fashioned by the

time it leaves the press; if he describes it with enthusiasm, a year or two later his enthusiasm may be proved unfounded, and therefore the reliability of the whole book may be brought into question. Dr. Herman has been fortunate in being able to discuss transurethral resection of the prostate in the light of the accumulated experience of himself and many other surgeons over a fair number of years. He has also written the most sensible discussion of that so popular drug, sulfanilamide, that has yet appeared in a book.

Dr. Herman evidently is primarily a doctor and secondarily a specialist in diseases of the genito-urinary tract: common sense permeates every page. He does not lose sight of his patient while treating his ailment. The book is recommended without reservation.

THE MANAGEMENT OF FRACTURES, DISLOCATIONS AND SPRAINS. By JOHN ALBERT KEY, B. S., M. D., Clinical Professor of Orthopedic Surgery, Washington University School of Medicine; Associate Surgeon, Barnes, Children's, and Jewish Hospitals, and H. EARLE CONWELL, M. D., F. A. C. S., Consulting Orthopedic Surgeon to the Tennessee Coal, Iron & Railroad Company, and the Orthopedic and Traumatic Services of the Employees' Hospital; Associate Orthopedic Surgeon to the American Cast Iron Pipe Company; Attending Orthopedic Surgeon to the Crippled Children's Hospital, St. Vincent's Hospital, South Highlands Hospital, Hillman Hospital and Children's Hospital, Birmingham, Alabama. Member of the Fracture Committee of the American College of Surgeons, American Academy of Orthopedic Surgeons and the Advisory Fracture Committee of the American Medical Association. Second Edition. 1246 pages, with 1222 illustrations. Price, $12.50. St. Louis: The C. V. Mosby Company, 1937.

When a book of more than 1200 pages goes into a second edition within 3 years the proof of the pudding is obvious. This book is written for the student, the general practitioner and the surgeon. The many illustrations are largely original in this text and have been carefully selected. The work is thoroughly practical and saturated with common sense throughout.

Dr. E. F. Fincher has revised Dr. Dowman's chapter on skull fractures and brain trauma and Dr. James Barrett Brown has revised his own chapter on fractures of the face and jaws. THE SOUTHERN SURGEON is proud that, though Dr. Key has not yet appeared in its pages, Dr. Conwell and his two contributors have, and it takes pleasure in recommending this book to everyone who has to manage fractures, dislocations and sprains.

INTRODUCTION TO OPHTHALMOLOGY. By PETER C. KRONFELD, M. D., Professor of Ophthalmology, The Peiping Union Medical College. 331 pages, with 44 illustrations. Price, $3.50. Springfield and Baltimore: Charles C Thomas, Publisher, 1938.

This book is intended to serve as a text for undergraduates who are under the direction of an experienced ophthalmologist with a wealth of clinical material at his disposal for teaching. The illustrations are therefore few: this fact makes it inadequate as a reference for the general practitioner and thus may interfere with its popularity. However, the author writes clearly, concisely and simply, and his text constitutes a wholly admirable "Introduction" to the subject.

PEDIATRIC SURGERY. By EDWARD C. BRENNER, M. D., F. A. C. P., Director of Surgery, Riker's Island Hospital and Detention Hospital; Attending Surgeon, Midtown Hospital; Associate Professor of Clinical Surgery, New York Post-Graduate Medical School, Columbia University; Associate Attending Surgeon and Chief of Clinic, Post-Graduate Hospital; etc. Former Surgeon Squadron A. 843 pages, with 293 illustrations. Price, $10. Philadelphia: Lea & Febiger, 1938.

The dictators overseas are making a big fuss over the young but one may suspect that this is largely because they are potential soldiers and mothers of soldiers. In this country the very young receive scarcely less attention: indeed one sometimes wonders if this idolatry is not a bit overdone. Professionally speaking, however, the difference in size is but a minor difference between a youngster and an adult: it is fitting that surgeons should recognize the many others.

Dr. Brenner does not take up fractures and dislocations, but he does describe adequately the other common surgical disorders of infancy and childhood, with chapters by specialists on anesthesia, blood transfusion, harelip, the thorax, urology and neurology. The importance of the preoperative storing of carbohydrate is emphasized, but one must object to the statement that 6 per cent dextrose is isotonic.

The book should prove a most valuable addition to the library of the surgeon who operates but infrequently on young people. However, the reviewer hopes that in future editions the many examples of surgical jargon will be replaced by English.

A MONOGRAPH ON VEINS. By KENNETH J. FRANKLIN, D. M., M. R. C. P., Tutor and Lecturer in Physiology, Oriel College; University Demonstrator of Pharmacology; Assistant Director of the Nuffield Institute for Medical Research, Oxford. 410 pages, with 45 illustrations. Price, $6. Springfield and Baltimore: Charles C Thomas, Publisher, 1937.

This is a most scholarly presentation of the whole subject of veins. It includes an historical chapter, a full discussion of physiology, a chapter on embryology by Keith Richardson, and a detailed discussion of the anatomy of the venous system. Although the clinical aspects are not dealt with in great detail, it should prove indispensable as a work of reference.

THE COMPLEAT PEDIATRICIAN. PRACTICAL, DIAGNOSTIC, THERAPEUTIC AND PREVENTIVE PEDIATRICS. *For the use of Medical Students, Internes, General Practitioners and Pediatricians.* By W. C. DAVISON, Professor of Pediatrics, Duke University School of Medicine, and Pediatrician, Duke Hospital; F. A. A. Pediatrics, F. A. C. P., etc. Second, Completely Rewritten Edition. 250 pages. Price, $3.75. Durham, N. C.: Duke University Press, 1938.

This book includes the most surprising amount of concentrated information, much of which is also important to those who do not treat children. Those who like their information very concisely presented, almost in tabular form, will welcome this practical volume.

Review *of* Neoplasms

formerly

The Review of Tumor Therapy

HILLYER RUDISILL, JR., M. D. *Compiler*

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SURGERY OF CARCINOMA OF THE COLON AND RECTUM

The surgical treatment of carcinoma of the large bowel has received a great deal of attention in the recent literature. Some of the points in diagnosis, operative technic and pathology seem worth reviewing.

The tardiness in diagnosis is illustrated by the figures of Stebbins and Burke.[1] Of 295 cases in the Wisconsin General Hospital only 125 were referred with the correct diagnosis in spite of the fact that in 180 cases a tumor could be palpated either abdominally or rectally. Eiken[2] reported from Denmark that of 1444 collected cases of carcinoma of the rectum 50 per cent were located from 4 to 10 cm. from the anus, thus in easy reach of the examining finger: yet the operability was only 27 per cent. Morton[3] states that in almost all cases of carcinoma of the anus, rectum, and rectosigmoid a proper digital examination will reveal the presence of the growth. He emphasizes examination in the stooping position and with the patient bearing down. Graham[4] points out two common diagnostic errors which are readily avoidable (1) bright red blood at stool and (2) persistent or so-called compensatory diarrhea. Any alteration in bowel habit in a patient of carcinoma age must lead to the suspicion of cancer until ruled out. Warthen[5] has noted the rarity of carcinoma of the colon in childhood. Morton[3] advocates that a proctoscopic examination should be a part of every x-ray examination of the colon. Case[6] points out the advantage of films in oblique positions to eliminate the overlapping shadows of rectum, sigmoid, and cecum.

Resection of the right half of the colon in one stage has been accompanied by a rather high incidence of peritonitis. Both Allen[7] and Pemberton and Whittaker[8] report improved results when a preliminary ileo-transverse colostomy is followed in about two weeks by resection of the growth at a second stage.

Lesions of the transverse and descending colon are most often treated by some form of exteriorization. Behrend[9] reports this to be the safest procedure in his hands. Bertrand, Etienne-Martin, and Corajod[10] have reviewed the indications and requirements of a successful Mikulicz operation.

In a recent editorial Harvey[11] emphasizes that a more rigorous technic is required in suturing the colon than the stomach or small intestine because of the infectiousness of its contents, the vulnerability of its blood supply, and the thinness of its walls. He therefore suggests that for those who persist in using catgut in the surgery of the large bowel, the Mikulicz procedure is the safer one. However, MacFee[12] at Cornell finds a much higher mortality for the Mikulicz operation than for resection with aseptic end-to-end anastomosis.

Lockhart-Mummery[13] has reported excellent results in 388 cases of carcinoma in the ampulla or lower part of the rectum treated by perineal excision. His operative mortality is 4.5 per cent in private cases and 10 per cent in hospital cases. The percentage of 5 year survivals is 52.5 per cent. In a smaller series Morton[3] also reported that posterior resection with or without colostomy gave the best numbers of 5 year arrests and the lowest operative mortality. Gehrels[14] doubts whether the higher operative mortality of the combined abdominoperineal resection is offset by a higher percentage of 5 year cures as compared to the sacral operation. However T. E. Jones[28] reports 54 combined abdominoperineal resections in one stage with only 4 deaths.

The use of preliminary colostomy in cancer of the left half of the colon continues to be emphasized. Von Haberer[15] employs a large catheter sutured in by the Witzel method. Devine[16, 17] performs a colostomy, usually at the hepatic flexure, with separation of distal and proximal loops. The completely "defunctioned" distal colon is irrigated for three or four weeks before removal of the growth at a second stage. Devine[17] describes his box clamp for closing aseptically the divided ends of the colon. Stone[18] has also described a new clamp of value in low sigmoid anastomosis since the holding handles can be applied at right angles to the clamp.

As regards pathogenesis the relation between polyps and carcinoma of the large bowel continues to receive attention. Mayo and Butsch[19] found that of 20 solitary polyps of the colon removed at laparotomy, 5 showed definite areas of adenocarcinoma. Brindley[20] found that 8 of his 306 cases of carcinoma of the large bowel had multiple primary growths in the colon. Spriggs[21] found 6 cases in which diverticulitis and carcinoma of the colon were associated.

Gordon-Watson[22] has summarized the evidence of the English workers on the origin and spread of cancer of the rectum. Five year survivals after perineal excision were 91 per cent of cases in which the growth was limited to the rectal wall and only 16 per cent when glandular metastases were present. He cites the studies of Dukes and Lloyd-Davies, based on 400 cases, which seem to show that about half the cases capable of cure by surgery can be eradicated as well by local excision as by total proctectomy.

Brown and Warren[23] reported 170 cases of rectal carcinoma with complete operative and postmortem findings and emphasize the importance of metastasis via the blood stream. They conclude:

> Sections of the primary growth in rectal carcinoma should be scrutinized carefully for invasion of capillaries or veins by tumor, because intravascular invasion frequently means visceral metastases, and its absence, provided at least three sections from different parts of the growth are examined, nearly always rules out visceral metastases. Its efficiency in predicting visceral or bone metastasis outranks that of neoplastic lymph nodes.

Eggers[24] notes that enlargement of lymph nodes seen at operation does not necessarily mean involvement by carcinoma.

The histologic type of colon malignancy varies somewhat with its location. Heyd[25] notes that adenocarcinoma predominates in the right half and scirrhous carcinoma in the left. Keyes[26] found that 27 of 470 cases of carcinoma of the rectum and anus were a squamous cell type.

Kirschner,[27] Gordon- Watson[22] and Gehrels[14] repeat the growing conviction that spread of carcinoma of the rectum is almost always upward and very rarely downward to involve the peri-anal structures. Gehrels and others, therefore, attempt to preserve the sphincter in the sacral operation on suitable cases.

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THE ENDOCRINE FACTOR IN RELATION TO CANCER

To the physician, either by the clinical experience which he has encountered or by the experimental evidence he has read, it is becoming increasingly more evident that the endocrine glands are in some way closely allied to the whole cancer problem. This attitude is justified if we realize that cancer is not a thing autonomous, but something which is definitely related to growth and metabolism. As long as the cell undergoes its normal growth and metabolism it is safe, but once abnormality occurs in these phenomena danger is encountered which eventually may lead to a malignant neoplasm.

Naturally the endocrine glands which are definitely related, the extent still unknown, to the growth and metabolism of the whole organism, must likewise be related to any abnormal disturbance in these mechanisms. So far some of the glands of internal secretion may be divided into two divisions in regard to their relation to the abnormal growth and metabolism of cancer. There are first those glands which seem to exert an antagonistic effect, namely the spleen, thymus, thyroid and adrenal, and secondly there are those glands which exert a stimulating effect in the development of malignancy, glands controlling the sexual activities of the organism, especially the ovary.

Up to the present we have to depend more on experimental evidence than on clinical in showing the various effects of these glands in their relation to cancer. In regard to the spleen as an antagonistic factor to cancer several interesting factors have been observed. It has been noted for a considerable time that metastases are rarely found in this organ, while the other organs of the abdominal cavity are frequently the sites of secondary involvement from the primary growth. Carrying out this observation on experimental animals it has been observed by some workers that it is impossible to graft malignant tumors in the spleen and furthermore the inhibitory action has been noticed on malignant grafts placed near the spleen. It has also been noted that splenectomy has been found to increase the susceptibility of animals to tumor transplants.

The thymus, a gland of which we know little, has however shown some evidence of likewise being an inhibitory factor to the development of cancer. Clinically the infrequency of epitheliomas in children has been noted, and experimentally thymectomy has been found to increase as much as four-fold the rate growth of tar cancer on the skin of animals. The thyroid has shown some evidence that its secretion exerts an inhibitory effect on malignant tumors. And finally injection into rats of the secretion of the adrenal gland mixed with certain iron salts has shown regression of malignant tumors. However the clinical evidence and the experimental results in regard to their antagonistic factor have so far not been extensive and conclusive enough to arrive at a clear understanding of the value of these glands in aiding the treatment of cancer, and complete eradication of cancer cells has never been observed using the extracts of these glands.

When we regard those endocrinologic factors which are related to the etiology of cancer we find extensive and numerous clinical and experimental observations. Before the beginning of the century clinicians began to wonder at the relation of the sexual glands to the

production of cancer. This resulted in numerous experimental procedures to establish this relationship. The gland chiefly involved has been the ovary and the hormone estrin, the product of the follicles of the ovary, also known as folliculin.

Furthermore the chief evidence of the etiologic relation between the ovary and cancer can be narrowed down to that between estrin and mammary gland cancer. The subordination of the histogenesis of the breast to the secretion of the ovary is well known and is brought forth during puberty, menstruation and pregnancy. But these are natural and normal phenomena, and while the breast is stimulated by estrin it is kept in a state of equilibrium by antagonistic hormones.

However, experimental evidence has long shown that continuous administration of estrin over a period of time, upsetting the hormonal equilibrium of the breast, results in hyperplasia and eventually cancer. This work has been aided by the discovery that certain strains of mice have a high degree of susceptibility to the spontaneous development of mammary cancer. On the other hand there are strains of mice which show low-tumor incidence.

If the ovarian hormone, in the small quantity ordinarily necessary to induce estrus, is injected continually into both high and low tumor strains an interesting phenomenon occurs. During the first four to six months growth occurs in the female breasts of both strains consisting of hyperplasia of the glands, resembling polycystic disease of the breast. But after that the high tumor strain shows more extensive and intensive growth gradually leading to the development of adenocarcinoma of the breast and the animal will be dead in about one year. The low tumor strain mice, on the other hand will not advance beyond the hyperplastic stage.

This development of adenocarcinoma of the breast occurs in the female mice and not as a rule in the male. But if young male mice of a cancer-susceptible strain are administered estrin before the adult regression of the male breast occurs, similar phenomena will appear as in the female leading to adenocarcinoma of the breast. Another interesting side light has been shown in this development. Breeding mice as a rule have a higher cancer growth rate than the non-breeding, probably due to the intense growth stimulus of pregnancy.

In considering this experimental evidence it is of course necessary to realize the importance of the hereditary factor. Indeed the estrogenic etiology must be considered subordinated to the hereditary one. But nevertheless interesting mechanisms are found underlying the combination of estrin and heredity, in being the spark which

ignites the development of mammary cancer. Experimental cancer due to this estrogenic hormone differs from others by being due to a normal product of the body to which the body is adapted. This development of cancer is the end stage of a continuous series of growth processes extending over a long period of time. And finally the cancer is not due to the formation of tissue caused by the stimulation of the hormone, thereby creating a favorable field for an unknown etiologic agent, but rather the hormone leads to the formation of new tissue because it stimulates the mammary gland and in stimulating the gland it leads to cancer formation.

Not only does estrin stimulate this cancerous development in the mammary gland, but it also exerts a proliferating effect in the vagina, cervix and in the beginning of the uterus. Continuous injection of large amounts of estrin lead to hyperkeratosis, and hyperpapillomatosis of the epithelium of the cervix uteri of the mouse. There is an increased down growth of the epithelium into the underlying connective tissue. While most workers in this research agree that this proliferation does not lead to true cancer, it does resemble a precancerous condition.

These changes in the vagina and cervix due to the action of estrin show a parallel action to those that occur in the mammary gland. Both appear spontaneous, but are really due to the action of estrin given under natural circumstances. However, the quantitative hereditary factor differs in the proliferation of the vagina and cervix from that of the mammary gland. Therefore the hereditary difference between strains is not due to the elimination of estrin from the body, but rather a difference in mode of response of the tissue stimulated. It has been suggested that this hereditary difference may be in part related to the ability to overcome the resistance of hyaline connective tissue and fat tissue to the development of proliferation and cancer.

It is natural in considering estrin a product of the ovary also to consider the hypophysis. We know that the ovary is controlled by the anterior lobe of the hypophysis and that in its turn it is effected by pregnancy, castration and the injection of estrin. Whether the anterior lobe of the hypophysis is enlarged by the injection of estrin is still questionable. There has been evidence found for and against this, by reliable authorities. But on the other hand, the hypophysis has shown definite relation to tumor growth both of hormonal and of other etiology. Multiple transplants of anterior and intermediate lobes of the hypophysis have shown increased incidence of mammary gland cancer without the simultaneous injection of estrin. Also in hypophysectomized rabbits the cutaneous application of tar or syn-

thetic hydrocarbon carcinogenic agents results in failure of growth of lesions beyond the cornified state, while controls developed papillomas and some epitheliomas. Therefore there is a justifiable hypothesis of the intervention of an hypophyseal hormone which permits tumoral growth.

Whether it is the practicing physician or the research worker, experimental data are of value only if it is possible to connect these results eventually with the human problem. It is a far cry from mice, rats, and rabbits to the human organism, and we have to be cautious in applying experimental findings in laboratory animals to explaining corresponding phenomena in the human body. However, there have been some clinical observations which bear out the relation of estrin to cancer which has been discovered in mice. Granulosa cell tumors associated with a disturbance in available estrin have resulted in precocious development of secondary sex characteristics in young girls. Endometrial hyperplasia and uterine fibroids have frequently been associated with a condition of multiple follicular cysts of the ovary in which there are no corpora lutea and therefore containing an excess of estrin. Furthermore it has been noticed that gynecomastia in the male and hypertrophy and tumor in the female breast are dependent on an estrogenic hormone leading to pathologic variations in the duct epithelium and surrounding breast tissue. Estrogenic principles have been found in the fibroadenomas of the breast.

This clinical observation of the relation of the ovary to the breast naturally leads to the value of surgical or radiation castration to relieve or to eliminate carcinoma of the mammary gland. Considerable work has been done with this in view since 1896 and the results show that in general it may be worth while if done before the menopause. However considering the seriousness of malignancy of the breast and the danger of both breasts becoming eventually involved, it can be considered that castration, in spite of its consequences, is rational. In one group of cases which have bone metastases from mammary cancer, radiation castration has shown definite benefit with relief of pain in 73 per cent of the cases treated and regression of the lesions in the bone in 30 per cent.

While we can see that the relation of endocrine glands to cancer is still in a chaotic state; nevertheless the theory of the hormonal etiology in cancer has to be seriously considered. It only involves a certain group of neoplasms and under very particular conditions, but the further understanding of the problem will go far in explaining the whole question of cancer etiology.

JOHN W. REGAN, M. D.

I. NEOPLASTIC AND NEOPLASTIC-LIKE GROWTHS OF LYMPHOID TISSUE

General Concepts and Terminology

The imperfect understanding of this group of diseases, and the variation in terminology make a discussion of general concepts and features useful. No attempt is made here to produce a scientific classification or explanation of the conditions, but the purpose is to point out the general trends of the principal types of these diseases, to indicate some of the well known interrelationships, and to correlate terminology with the outstanding manifestations and forms, listing synonyms for terms favored here. In numerous publications detailed accounts of clinical and pathologic manifestations of the conditions can be found, and such details will not be included here.

Terminology for the Disease Group

There is no simple term which may be applied with exactness to the group as a whole, and the several terms used previously in that fashion are now regarded as obsolete. Lymphoma is defined as "A tumor composed of lymphoid tissue" (Stedman's Medical Dictionary, 13th Edition), and as such it can be applied to the group of diseases in the sense that there is swelling or increase in size of lymphoid tissue, but it does not indicate either the variety or the components of lymphoid tissue which are involved. Lymphoblastoma was defined by Mallory as "A tumor of mesenchymal origin of which the cells tend to differentiate into lymphocytes, that is, into cells of the lymphocytic series". This term was applied to the whole group of tumor and tumor-like conditions of lymphoid tissue, but it is now obvious that the lymphocyte is not the only cell involved. Malignant lymphoma has been applied to the diseases as a group, and to Hodgkin's disease as a type, adding to the confusion.

Lymphoblastoma has also been applied to localized slow growing tumors of the lymph nodes composed of large round cells, apparently originating in the germinal centers. Rate of growth and extension are slow usually, but some cases develop into neoplasms in the form of lymphosarcoma, which soon or late produce death. It is probably best to regard such a growth as a lymphosarcoma of low grade malignancy. Follicular lymphoblastoma is a term more accurately descriptive. Actually a neoplasm of lymphoid tissue can be said to be benign only when it has remained localized throughout the life of the individual and has not contributed to his death through its growth alone.

In our present state of ignorance regarding the true nature of these diseases a reasonable view is that of Callender, to call them

tumor and tumor-like conditions. For the individual group types the desirable term would be one which indicated etiology, the tissue involved, and the prime manifestations. Since etiology is not known, the terms selected can only include the last two provisions; for example, lymphosarcoma, a malignant tumor of lymphocytes (or their precursors), and aleukemic lymphocytoma, and overgrowth of lymphocytes (or their precursors) which do not appear in the blood stream in appreciable numbers. Unavoidably each term develops certain implications.

Normal Situations and Components of Lymphoid Tissue

To understand the sites of growths of lymphoid tissue one must have a general idea of the distribution of lymphoid tissue in the body. Most obviously it makes up the lymph nodes, tonsils, thymus, the Malpighian corpuscles of the spleen, and the solitary and conglomerate follicles of the gastro-intestinal tract. Minute patches are found in the portal areas of the liver lobules, in the lung, the skin, and the bone marrow; in fact, there are probably minute patches of lymphoid tissue in every organ or structure of the body. Theoretically and actually primary tumor and tumor-like growths of lymphoid tissue may occur wherever lymphoid tissue is present, but there are sites where the overgrowth commences more frequently.

The components of lymphoid tissue with which this discussion is concerned are the mature lymphocytes, scattered through lymphoid tissue, the immature lymphocytes, the so-called lymphoblasts of the germinal centers, and the reticular tissue, a supporting tissue composed of elongated and branching cells related to a fine network of fibers, the latter characterized by their affinity for silver stains. This reticular tissue is distributed diffusely in lymphoid tissue, less densely in the germinal centers, and it is also present in the spleen and the bone marrow, in the liver (Kupffer cells), as well as in the skin, lung, and other tissues, both related and unrelated to the lymphocytic elements of these tissues. The reticular tissue supplies at least a portion of the monocytes of the blood.

The Reactive or Infectious Growths

The components of lymphoid tissue may proliferate in response to bacterial or virus stimulation, as exemplified by the granulomatous growths in tuberculosis, leprosy, and lymphogranuloma inguinale. Apparently the reticular tissue plays the major role in these instances. Certain so-called non-specific types of reactive hyperplasia are termed pyogenic granulomas, a rather poor term which implies that pyogenic bacteria of low virulence furnish the stimulus for proliferation. In these conditions, while the extent of

the growth varies, continuance of growth depends upon continuance of stimulation, and removal of the etiologic agent causes cessation of growth.

Infectious mononucleosis affords one of the most interesting examples of an extreme degree of proliferation of lymphoid tissue, which is a response to an apparently infectious agent. The generalized glandular enlargement with the presence of great numbers of mononuclear cells in the blood stream plus the fever and rather limited course is quite familiar. The comparatively immature or mature cells in the blood stream are either of the lymphocytic or reticulocytic type. The disease invariably subsides after pursuing a characteristic course, but during the height of the leukocytosis the differentiation between leukemic lymphocytoma (lymphocytic leukemia) and leukemic reticulocytoma (monocytic leukemia) may be difficult hematologically. The lymph nodes are enlarged and are overrun with large immature cells which are derived from either the germinal centers (lymphoblasts) or the reticular tissue (reticulocytes), but the microscopic architecture of the lymph nodes is never completely eradicated, and the capsules are never penetrated by the proliferating cells.

Tumor-Like Growths—Leukemias

Comparable forms of the lymphocytic and the reticulocytic (monocytic) types of leukemia exist. The rate of proliferation of the cells is of all degrees, so that the specification of acute or chronic forms indicates acuteness or chronicity in an extremely general manner only. The hematologic differentiation between the forms is a problem in itself, and an opinion is of value only in the hands of an experienced hematologist. That the rate of cellular proliferation does not necessarily remain constant through the course of a given case further complicates the picture. In addition, in either type, as in myelocytic leukemia, the proliferating cells may be cast into the blood stream in great numbers, or may be retained almost entirely in the tissues, giving the leukemic and the aleukemic forms, respectively.

There is usually generalized lymph node enlargement in the leukemias but there are forms in which for a time at least the enlargement is local, and in the usual case of generalized enlargement, certain groups of nodes may be especially prominent.

The course may be so prolonged that for years the activity of the victim is not hampered, or it may be so rapid, that the time from discovery to death is but a few days. In general the leukemic forms run a more active course, and usually the very acute cases occur in the young or the elderly.

General Patterns of These Leukemias

For both the lymphocytic and the reticulocytic types of leukemia there are the leukemic and the aleukemic form. For example, in the lymphocytic type, the proliferating cells may be present in the blood stream up to several hundred thousand per cubic millimeter, or they may remain in the tissues. Actually in the aleukemic forms of the disease some of the undifferentiated forms are present in the circulating blood, and may be detected in stained smears, but the total number of cells of the lymphocytic series is not increased. The same concept holds for the reticulocytic type of leukemia (also for the myelocytic type). All gradations as to quantity and differentiation of the proliferating cells in the blood stream occur. The leukemic manifestations of the neoplastic conditions (lymphosarcoma and reticulum cell sarcoma) will be mentioned below.

Correlation of Leukemic Characteristics and Terminology

The concepts of these growths so far is quite simple and orderly. The term lymphocytoma and reticulocytoma are applicable in that they refer to an overgrowth of the specified cell type, with some of the features ascribed to neoplasms. Furthermore, these terms can be amplified to indicate the presence or the absence of leukemia, without producing such a contradictory term as aleukemic lymphatic leukemia. The following terms are therefore developed; leukemic lymphocytoma and aleukemic lymphocytoma, leukemic reticulocytoma and aleukemic reticulocytoma. Each has several synonyms which will be listed below.

An outstanding but confusing feature of the leukemias is the decided tendency for the proliferating cells not only to infiltrate tissues other than lymphoid tissue, but apparently to proliferate in the sites of infiltration—one of the outstanding characteristics of malignant neoplasms. In some instances the proliferation both within and outside of lymphoid tissue produces masses of appreciable size, and that manifestation may overshadow the leukemic feature. This characteristic is designated by the use of the suffix -oma.

Neoplastic Growths of Lymphoid Tissue

Lymphosarcoma: This appears to be a primary neoplastic overgrowth of cells of the lymphocytic series, which may be localized and remain so for years (follicular lymphoblastoma?), but with the potentiality of developing invasive malignant qualities; it may commence as a localized growth and then invade and metastasize; or it may appear from the beginning to be a generalized neoplastic

growth at usual sites of lymphoid tissue in the body. The lower grade forms of the definitely malignant types are composed of small round cells which represent adult type lymphocytes, and the forms of higher grade malignancy are composed of cells approaching the lymphoblasts in appearance.

Leukosarcoma: Perhaps a term more applicable would be leukemic lymphosarcoma, for here is one of the conditions indicating a close relationship between lymphocytic leukemia, a tumor-like growth, and lymphosarcoma, a neoplastic growth. Sometimes spontaneously but more frequently following irradiation of apparently typical lymphosarcoma, a severe leukemia of the lymphocytic type will develop. There are also instances of the reverse manifestation; leukemic and aleukemic lymphocytoma may develop the characteristics of lymphosarcoma at the expense of the previous characteristics.

Reticulum Cell Sarcoma: Formerly designated the large cell type of lymphosarcoma, this is now considered a neoplasm of reticular tissue. The cells are of more or less uniform characteristics in a given instance, and in different cases may be round, oval, elongated or tend to branch, but in all instances the cells are built upon a delicate network of reticular fibrils. Most commonly this tumor first appears as a local growth of lymph nodes or lymphoid tissue, and then invades and metastasizes. Common sites of origin are the groups of peripheral lymph nodes, the nodes of the mediastinum or the abdominal cavity, or the lymphoid tissue of the gastrointestinal tract. Rarely a reticulum cell sarcoma will develop leukemic manifestations.

Hodgkin's Disease: This condition, of which there are several forms, is considered now to be an overgrowth of reticular tissue, but it is characterized by a peculiar and quite typical cellular pleomorphism, which is the criterion for separating this group from the other forms of reticular tissue overgrowth. Because of the lack of a better term, and because usage has rendered it familiar, the term Hodgkin's disease is probably best retained. Recent conceptions indicate that the localized form of the overgrowth, which tends to sclerosis, is a reactive hyperplasia of the reticular tissue, supposedly in response to an agent which some consider infectious. This form may also rarely terminate as a sarcomatous growth.

There is a generalized form of Hodgkin's disease which is comparable to the aleukemic form of reticulocytoma, but presents the bizarre cellular pleomorphism associated with reticular fibril production, by which the forms of Hodgkin's disease are characterized. This form more frequently than the former terminates as a sar-

coma. It is also characterized by the presence of appreciable numbers of reticulocytes (monocytes) in the blood, although this does not often assume the proportions of a leukemia. There are instances, however, where Hodgkin's disease has terminated as an acute mononuclear (probably reticulocytic) leukemia.

Hodgkin's sarcoma is rare, or at any rate it is but rarely diagnosed by clinicians, hematologists, or pathologists. The cellular picture is variable but the pleomorphism of generalized forms of Hodgkin's disease tends to be present, and these tumors are considered neoplastic growths of reticular tissue, as evidenced by the production of an abundance of reticular fibrils. They may be thought of as a reticulum cell sarcomas evidencing marked cellular pleomorphism. The main reason for grouping them under a separate heading is because the cellular picture does not conform to the more differentiated forms of reticulum cell sarcoma, and not improbably the grouping of these conditions will vary in the near future.

Terms Preferred in This Paper	Synonyms
1. Infectious mononucleosis.	a. Glandular fever. b. Acute mononucleosis.
2. Lymphosarcoma (low grade).	a. Follicular lymphoblastoma. b. Lymphoblastoma. c. Lymphoma.
3. Leukemic lymphocytoma.	a. Leukemic lymphadenosis. b. Lymphatic leukemia. c. Lymphocytic leukemia.
4. Aleukemic lymphocytoma.	a. Aleukemic lymphadenosis. b. Aleukemic lymphatic leukemia. c. Aleukemic lymphocytic leukemia. d. Lymphatic pseudoleukemia.
5. Leukemic reticulocytoma.	a. Monocytic leukemia.
6. Aleukemic reticulocytoma.	a. Aleukemic monocytic leukemia. b. Monocytic pseudoleukemia.
7. Lymphosarcoma.	None.
8. Leukemic lymphosarcoma.	a. Leukosarcoma.
9. Reticulum cell sarcoma.	a. Large cell lymphosarcoma.
10. Hodgkin's disease.	a. Malignant lymphoma. b. Pseudoleukemia. c. Anemia lymphatica. d. Lymphosarcoma. e. Lymphadenoma. f. Aleukemic reticulocytoma (cells pleomorphic—generalized Hodgkin's), etc.
11. Hodgkin's sarcoma.	a. Reticulum cell sarcoma (cells pleomorphic).

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